

SPECIAL ISSUE: Diet, Health and the Food Supply

SCIENTIFIC AMERICAN

The
Threat of
**TAINTED
FOODS**

page 112

September 2007

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FEAST and FAMINE

The Global Paradox of Obesity and Malnutrition

Not Just Calories

Complex Causes
of Weight Gain

Gene Tech

Can It Help End
World Hunger?

Chocoholic

Neuroscience of
Food Addictions

Pounds of Cure

Healthier to Be Overweight?



SPECIAL ISSUE

Feast and Famine

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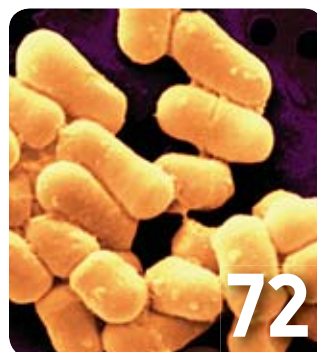
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How can the poorest countries fight obesity?

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Cover by Kenn Brown (illustration), James Porto (photography and photocomposition) and Brett Kurzweil (food styling).

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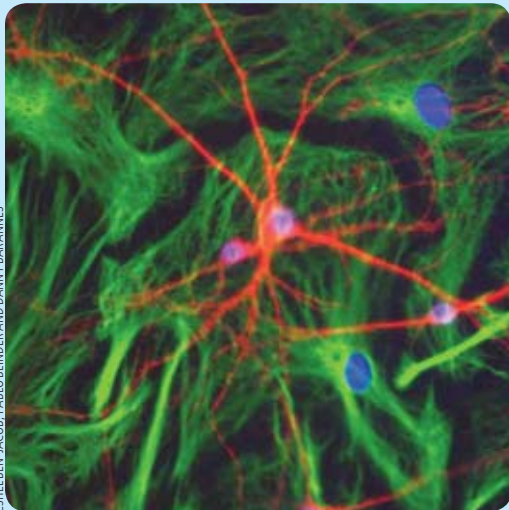
Safe to Grow—and Eat?

Transgenic crops could help feed a hungry world, but they are controversial. Why? Go to www.SciAm.com/ontheweb

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CULTURED NEURONS (*below*) grown atop a polymer panel studded with electrodes were induced to encode persistent

memories for the first time ever. The results augur a future in which neurons living outside the body will communicate with computer chips to process information in novel ways.



ESHEL BEN-JACOB, PABLO BLINDER AND DANNY BARANIN

LIKE WHAT YOU SEE? Everything pictured here, plus Web-exclusive supplements to the articles in this issue, is available at www.SciAm.com/ontheweb

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NICO SMIT (StockPhoto (hyaena); CHRISTINE GONSALES (StockPhoto (water buffalo); ISTOCKPHOTO (lion)

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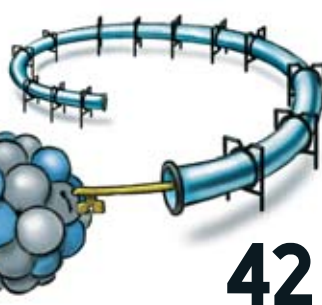
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All You Can't Eat

The paradoxes of the modern diet need to be tamed



If our civilization should someday collapse, then—with apologies to McDonald's—let this be its epitaph: “Billions and billions served.”

Humanity has come a long way from its hunter-gatherer roots. Thanks to industrial-age agricultural production, global commerce and the 20th century's green revolution in farming, the world can support billions of people who once would not have found enough to eat. But goodness, look what we're feeding them.

Modern culinary extravaganzas include high caloric fantasies lacking even a twig's worth of nutrients, and poor nations are among their most avid consumers. Widespread obesity and malnutrition exist side by side—sometimes even within the same people. The world has become a place simultaneously of overabundance and aching starvation: the cornucopia and the empty cupboard in one.

In this special issue, *SCIENTIFIC AMERICAN* explores the relation between human health and food, which has never been more complicated and paradoxical.

After gobbling down mountains of chips, rivers of cream, stampedes of beef and poppin' fresh boxcars of baked goods, many of us fret over which best-selling diet book can salvage our health and help us see our toes again. Are we expecting too much? Nutritionist Marion Nestle says yes. In “Eating Made Simple” (beginning on page 60), she lays out why the state of nutritional science is still too incomplete to make detailed prescriptions for individual well-being. Journalist Paul Raeburn, in his contributions (“Dropping Weight... and Keeping It Off,” on page 66, and “Can Fat Be Fit?” on page 70), also deflates expectations about how well

weight-loss diets work and how many extra pounds we can pack without risk. The traditional advice in favor of exercise and moderation still applies: take the stairs, leave the cannoli.

At the physiological level, we are almost unchanged from our hunter-gatherer ancestors. We carry elaborate regulatory circuits in our heads and guts that helped us survive back when periodic famine was common and sweet, fatty desserts were not. The article from Jeffrey S. Flier and Eleftheria Maratos-Flier (“What Fuels Fat,” on page 72) and the interview with Nora D. Volkow (“This Is Your Brain on Food,” on page 84) explain what those holdovers mean for us today.

Barry M. Popkin, in “The World Is Fat” (page 88), and Per Pinstrup-Andersen and Fuzhi Cheng, in “Still Hungry” (page 96), describe the nutritional Scylla and Charybdis through which developing nations now navigate. Populations that escape famine by filling their bellies with cheap snacks and soda set themselves up for different sets of health concerns in the future. A controversial remedy for hunger might be to embrace genetically modified crops; Terri Raney and Prabhu Pingali suggest as much in their piece (“Sowing a Gene Revolution,” on page 104).

The public has become acutely aware that the food supply is increasingly vulnerable, both to terrorist actions and to accidental contamination. Check out “Is Your Food Contaminated?”—Mark Fischetti's sobering overview of the situation and of the technological fixes that might help restore a measure of security, starting on page 112.

Then maybe pass on that second helping of potatoes and take a brisk walk to think it all over.

JOHN RENNIE
editor in chief



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LETTERS

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Martian Molecules ■ Cancer ■ Quantum Theory



MAY 2007

■ Dubious Disclaimer?

I applaud *Scientific American's* decision to publish Peter Duesberg's article on cancer ["Chromosomal Chaos and Cancer"] despite consensus against his belief that HIV is not linked to AIDS. I was disappointed, however, to find the editors apologizing for doing so in "When Pariahs Have Good Ideas" [Perspectives].

The beauty of science is that it is not predicated on trust. Repeatable experiments render the messenger irrelevant. If the science of a body of work is solid, it deserves publication regardless of who produced it. Further, it is my understanding that Duesberg's cancer research remains reputable. Do we consider Michael Jordan any less a basketball player because his performance at baseball was sometimes less than stellar? Although I may disagree with Duesberg's premise regarding HIV, I believe no one's work should be discounted simply because he or she has held an unpopular opinion.

Ethan Gutierrez
Embudo, N.M.

THE EDITORS REPLY: *We do not apologize for publishing "Chromosomal Chaos and Cancer." But as considerable mail and online commentary have demonstrated, not all readers are as fair-minded as Gutierrez in separating Duesberg's work on cancer from his denial of the realities of HIV. We did not want anyone to misinterpret—or misuse—his Scientific American article on the former as a tacit endorsement of the latter. Conversely, we also did not want anyone to skip Duesberg's article out of*

"If the science of a body of work is solid, it deserves publication regardless of who produced it."

—Ethan Gutierrez EMBUDO, N.M.

scorn for his HIV denial. We therefore chose to make our positions clear in the Perspectives column.

■ Cancer and Complexity

Duesberg gives an informative and different perspective of aneuploidy as a possible cause of cancer, but in the process he makes unwarranted attacks on the theory of gene mutation as a cause. Although gene mutation alone cannot explain cancer fully, its role in many cancers cannot be overlooked. Cancers are robust, heterogeneous systems with multiple causes and in general involve the complex interplay between the immune system, the aging process, epigenetics, gene mutation and aneuploidy. Any simplistic theory like the gene mutation theory that Duesberg paints cannot possibly explain all the observed characteristics of cancers, and his alternative aneuploidy theory is no exception. (For example, Duesberg asserts that the gene mutation theory cannot explain the long latency in carcinogen-caused cancers, but aneuploidy evolves faster than gene mutation, making his theory even less likely.) Gene mutation and aneuploidy can work hand in hand in carcinogenesis. One does not have to discredit the prevailing theory to find the cause of the disease.

Wai Wong
Mitcham, Australia

■ Oxygen Link?

I believe that the two possible sources of methane on Mars presented in "The Mystery of Methane on Mars and Titan,"

by Sushil K. Atreya, should release three atoms of oxygen for every molecule of methane, but Atreya does not mention oxygen. Has thought been given to testing for a corresponding amount of oxygen to corroborate these sources?

Stephen R. Troy
Arnold, Md.

ATREYA REPLIES: *Production of methane requires a reaction between carbon and hydrogen. Oxygen, though unnecessary, can be involved if it is incorporated into the reacting molecules. A key reaction between four carbon monoxide and two water molecules would*

CREATING AN ATMOSPHERE: Mars's methane derives either from living bacteria or from a rock-water reaction called serpentinization.

seem to ultimately result in three oxygen atoms and one methane molecule. This is somewhat misleading, however, because oxygen atoms form oxygen molecules and also destroy methane and other organics. Thus, on Mars oxygen most likely partitions into formaldehyde, methanol, peroxides, carboxylic acid or another form on reactions with ambient minerals, gases and fluids. Unless the source of these oxygen-containing molecules is continuous or they are sequestered in the soil or rocks, the detection of these molecules would be difficult because of their short life span. Nevertheless, the mass spectrometer on the Sample Analysis Suite of the 2009 Mars Science Laboratory can detect very small amounts of gases, either directly or after releasing them from solids by pyrolysis.

On Titan, extremely low temperatures in the interior, surface and atmosphere allow only very basic oxygen reactions. The best hope of finding oxygen-bearing molecules—discounting small amounts of carbon monoxide and carbon dioxide in the air—is on the surface. The Huygens probe's gas chromatograph mass spectrometer was able to measure the gases evaporated from Titan's icy surface, which are currently being analyzed. Any future missions to Titan will be well served

by paying close attention to its surface material.

■ Quantum Query

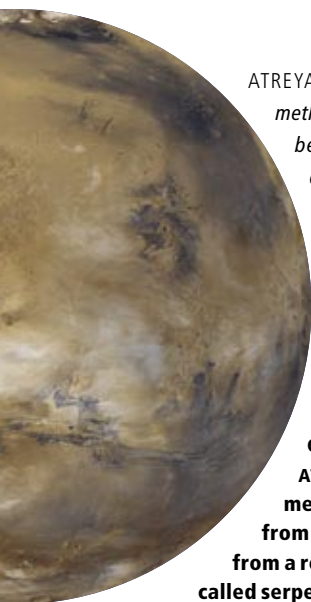
According to “A Do-It-Yourself Quantum Eraser,” by Rachel Hillmer and Paul Kwiat, the interference pattern created when a photon can travel through either of two slits is destroyed by knowledge of which path it took. But if only one observer gains this knowledge, is the effect the same for other observers?

Also, as nothing can be measured with total accuracy, is everything in quantum flux, without definite size or shape?

John S. Somerset
Birmingham, Ala.

KWIAT REPLIES: *Quantum interference does not actually depend on any observer. To lose interference in the two-slit experiment, it is sufficient that the “which path?” information could be obtained by some hypothetical observer, even if none existed.*

As to the second question, there are some things we can measure with complete accuracy, such as the number of atoms making up a particular molecule, which can be counted. Other quantities are con-



strained by Heisenberg's uncertainty principle, which tells us that better knowledge of one thing automatically implies poorer knowledge of something else. Further, the intrinsic wave nature of all particles does imply that no object has a true "hard edge." (Even in a simple hydrogen atom, the location of the electron is smeared out around the nucleus, with an exponentially decreasing likelihood of finding it the farther away it is from the proton.)

ERRATUM "Medieval Quasicrystals," by JR Minkel [News Scan], includes a photograph of tile work from a Turkish mosque incorrectly identified as an example of a quasicrystal, a complex pattern that never repeats. Tile work from the Darb-i Imam shrine in Isfahan, Iran, which forms a pattern that repeats but could be extended to make a quasicrystal, can be seen at www.SciAm.com/ontheweb

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Crick's Progress ■ Flight Incentive ■ Flame Tamer

Compiled by Daniel C. Schlenoff

SEPTEMBER 1957

DNA—"It is difficult to resist the conclusion that DNA is genetic material. If that is the case, our problem is to learn how DNA reproduces itself. The double-helical structure of DNA suggests a possible answer, which I have discussed in a previous article. The basic idea is that the two chains of the DNA, which fit together as a hand fits into a glove, are separated in some way and the hand then acts as a mold for formation of a new glove while the glove acts as a mold for a new hand. Thus we finish up with two gloved hands where we had only one before. In chemical terms we imagine that monomers supplied by the cell align themselves along the mold chain with complementary bases pairing up. —F.H.C. Crick"

PUGWASH CONFERENCE—"For six days last July, 22 scientists from 10 countries met in the hamlet of Pugwash in Nova Scotia to talk about 'the perils to humanity posed by the development of weapons of mass destruction.' Financed by the Cleveland industrialist Cyrus Eaton, a native of Pugwash, the conference was the culmination of an appeal for such a meeting made two years ago by Albert Einstein and Bertrand Russell. The group includes scientists from the U.S., the U.S.S.R., China and Japan. They began by agreeing to 'say nothing which might seem to favor one rather than the other of the two great groups of powers into which the world is divided.'"

[EDITORS' NOTE: The latest on Pugwash Conferences is at www.pugwash.org]

SEPTEMBER 1907

GLORIOUS FOOD—"The dietetic vice of a century ago—the time of the three-bottle men—was alcoholic; now, we Americans, at least, eat too much, especially too much meat. It is the concomitant of our prosperity. And to this effect Prof. Chittenden

submits a most valuable and scientific work in which are detailed exhaustive experiments done through six years by him and his colleagues at Yale. He concludes that the dietary standards are much too high; and that better health, increased efficiency, and greater chances of longevity would certainly follow upon our reducing our proteids at least fifty per cent."



WATER METER (needs miniaturization), 1857

AERO TROPHY—"Nearly four years ago the Wright brothers, in this country, announced the successful application by them of a gasoline motor to an aeroplane. No public demonstration has ever been made by them, however; and although, according to their own statements and those of eyewitnesses, they have solved the problem, still many people doubt this. At any rate, it is probable that progress in the new science will be made by others, and that in time there will be several kinds of heavier-than-air machines perfected. It is with the idea of encouraging inventors in this line by giving them a valuable object of art worth winning, that the Scientific American trophy has been completed

and presented to the Aero Club of America. The trophy commemorates Langley's aerodrome, which was the first motor-driven model aeroplane to make a successful flight of over half a mile."

SEPTEMBER 1857

COUNTING WATER—"Liberal supplies of water in cities are a blessing which cannot be too highly appreciated. To prevent waste, however, there is a necessity of some method of recording the quantity used in each household or establishment. The meter represented in the accompanying engravings is so arranged as to require no packed parts, to work practically independent of friction, and to afford a means of measuring with great accuracy whether the flow be rapid or extremely slow."

TELEGRAPH CONTROL—"The news burst on India like a thunderclap that the native regiments at Meerut and Delhi had mutinied, murdered their officers, massacred all the English inhabitants of Delhi, placed the King of Delhi on the throne and threatened the empire. All this happened on the 11th of May. On the 13th it was known by telegraph to Europeans only throughout India—I say to Europeans only, for immediately the post was stopped, and an embargo placed on all native correspondence. It is not too much to say that the telegraph saved India. —*London Times*"

THE HOTTEST STYLES—"Many ladies have been burnt to death by their light gauze and cambric dresses taking fire and blazing up before there was time to extinguish the flame. Actresses and *danseuses* are most liable to this, and the talented Clara Webster and others lost their lives this way. It ought, therefore, to be generally known that by steeping the dress, or material composing it, in a diluted solution of chloride of zinc, it will be rendered perfectly fire-proof."

Cyberwarfare ■ Surviving Supervolcanoes ■ Better Biofuel ■ House Cat Origin

Edited by Philip Yam

■ First Strike

Is bombing an air base equivalent to hacking into its computer system? Both can cripple the base, but is a software strike an act of war? That is what NATO wants to decide fast, after the first recognized cyberassault in the world—on Estonia, one of its member states.

This past April and May many of Estonia's government and banking Web sites came under heavy network attack, ostensibly orchestrated by the Russian diaspora in various countries and by the minority Russian population in Estonia. They were apparently protesting Estonia's moving of a Soviet war monument from the center of Tallinn, the nation's capital, to a war cemetery. The attackers hijacked millions of computers worldwide by sneaking in "bots"—programs capable of wresting control of the machines and turning them into unsuspecting foot soldiers of cyberwar. The computers then overloaded Estonian servers with false requests. This invasion resembled the Code Red attacks in 2001, which deployed close to a million bots [see "Code Red for the Web"; SciAm, October 2001]. This time the silicon army exclusively targeted the government infrastructure of a country, which by most other means would constitute an act of war.

Not having a policy on this unprecedented "cyberterrorism," NATO member states could do little to aid Estonia, which joined in 2004. That should change soon: in June, NATO representatives met in Brussels and assigned top priority to drafting a policy on cyberwarfare. No one expects that the effort will be simple.

—Sourish Basu



■ Blast in the Past

A supervolcanic eruption packs the punch of a small asteroid slamming into Earth [see "The Secrets of Supervolcanoes"; SciAm, June 2006]. Some researchers hypothesize that these rare geologic cataclysms could throw up enough ash to affect climate and wipe out local populations. Scientists analyzing the remnants of a supervolcanic eruption that occurred 74,000 years ago in Toba, Indonesia—the largest in the past two million years—report in the July 6 *Science* that it did not drive away early humans. At a site in southern India, the team found ancient stone blades dating to before and after the Toba eruption. The blades show technological continuity, indicating that the locals survived the nearby release of 2,800 cubic kilometers of magma and 800 cubic kilometers of ash.

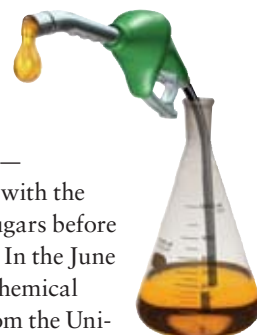
■ Ethanol Alternative

The biofuel called 2,5-dimethylfuran, or DMF—made by adding acids to glucose or fructose—packs 40 percent more energy than ethanol, bringing it on par with gasoline [see "Is Ethanol for the Long Haul?"; SciAm, January 2007]. And unlike ethanol, the compound does not become contaminated by absorbing water from the air. But getting rid of an intermediate compound that forms in the DMF reaction, called 5-hydroxymethylfurfural

(HMF), has been troublesome—HMF reacts with the remaining sugars before the acid can. In the June 21 *Nature*, chemical engineers from the University of Wisconsin—Madison describe how the addition of liquid hydrocarbon quickly draws HMF to it. Hydrogen and another catalyst can then turn the HMF into DMF. Such catalytic reactions are simpler and more efficient than the fermentation methods used to make ethanol, although researchers need to evaluate the environmental effects of DMF.

■ Meow Power

Genetic analyses have revealed how felines have clawed their way around the world [see "The Evolution of Cats"; SciAm, July 2007]. The latest DNA study concludes that today's 600 million house cats descended from five maternal lineages of a Near Eastern wildcat, *Felis silvestris lybica*, whose relatives today include the Scottish wildcat (*photograph*). The study, published online June 28 by *Science Express*, confirms that feline domestication took place in the Fertile Crescent, probably some 10,000 years ago, when humans began farming and most likely looked to cats to control grain-robbing rodents.



MATTHIAS KILKA (zeta) (Corbis); LAWRENCE MANNING (Corbis); EMILY HARRISON (photocomposition); ALAN MARSH (Design Pics/Corbis); EVAN MACDONALD (iStock)

PUBLIC HEALTH

Suffering a Slow Recovery

Failed rebuilding after Katrina sets off a mental health crisis in the Gulf **BY EMILY HARRISON**

There may be a new roof on the New Orleans Superdome and tourists in the French Quarter, but time is not healing all wounds in the wake of Hurricane Katrina. On the contrary, time has been a salt in the psychological wounds of hundreds of thousands of Gulf Coast residents. Even two years after the storm, mental health problems in the region are growing among the nearly 70,000 families still living in temporary housing provided by the Federal Emergency Management Agency (FEMA). The slow recovery, researchers and clinicians are finding, has bred levels of mental distress unseen in the aftermath of other disasters.

"Most of the time, distress emerges early and dissipates over the first year post-disaster," says psychologist Fran Norris

of the National Center for Post Traumatic Stress Disorder at Dartmouth Medical School. Not so with Hurricane Katrina. One year after the storm a Harvard Medical School committee funded by the National Institute of Mental Health reported doubled rates of depression and anxiety in the region. A team led by David Abramson of the National Center for Disaster Preparedness (NCDP) at Columbia University, in collaboration with the Children's Health Fund, surveyed residents of FEMA-provided trailers and hotels in Louisiana and reported widespread clinically diagnosed psychiatric problems. Sixty-eight percent of female caregivers and 44 percent of children suffered new mental health issues, including depression, anxiety and sleep disorders. When

the Columbia team surveyed a similar group in Mississippi six months later, it found even higher rates of distress despite the fact that Mississippi had suffered less damage and had an additional half a year to recover. Clinical care providers corroborate the studies' findings, both sets of which were scheduled to have been updated by mid-August.

"A disaster is an abnormal event, and people being affected by that is normal," allows Anthony Speier of the Office of Mental Health at the Louisiana Department of Health and Hospitals. "But Katrina falls into the realm of a catastrophic event. We are not set up to help a population recover from that," he adds.

Katrina differs from other storms not only for its sheer magnitude but also for the stymied rebuilding efforts following it. The federal disaster area spanned the size of Great Britain, at least 1,836 people perished and some 1.5 million people were displaced, creating the largest population migration in the U.S. since the dust bowl of the 1930s. Enticing people back to their neighborhoods without health, educational or criminal justice systems to support them there is difficult, so most neighborhoods have remained deserted in gray shambles with negligible visible change in the past year, according to Speier.

This open-ended holding pattern and continued displacement have perpetuated feelings of loss of control, which correlate with depression and anxiety. "Many people still live in conditions and with uncertainties that would rarely still be present nearly two years after a disaster," Norris says.

This storm was particularly cruel in that it hit people with very few resources



SWEPT AWAY: A homeowner in New Orleans stands on the only remnant of his dwelling after the Hurricane Katrina disaster. Slow rebuilding efforts are putting displaced residents under emotional stress that authorities did not anticipate.



TRAILER LIFE, such as that in New Orleans's Lower Ninth Ward, has incubated feelings of isolation and despair.

very hard. For many it took away not only their home and friends but also their social identity, job and any sense of self-sufficiency. Abramson and NCDP director Irwin Redlener note that of those they surveyed who had annual salaries of \$10,000 or less before the storm, 53 percent were

still out of work a year after it. Rents have doubled, though, and the FEMA trailer parks where many now indefinitely reside have proved to be pressure cookers for despair. People feel unsafe among their neighbors and isolated from the rest of the city, and the density of depression, Abramson observes, has a community-level, spiraling effect.

These assessments bear political significance because federal disaster spending is based on the assumption that once an area's infrastructure recovers, the population will recover naturally. Direct compensation for loss is one of the lowest priorities, practically nonexistent for individuals who owned no property to begin with. And the Stafford Act, which allows for short-term mental first aid after a disaster, is not designed to support long-term therapies that help to overcome persistent distress.

Mental health investigators favor a recovery policy that goes even beyond long-term counseling to support organizations and initiatives that help communities rebuild themselves. "It makes sense that if

one of the problems people experience after disasters is loss of control, which is highly related to mental health problems, then having a vehicle for regaining at least some control would be helpful," Norris says. Several grassroots efforts and micro-redevelopment plans have succeeded in a few communities, but scaling them up will require broader support.

Meanwhile, experts say, sending a public message that balances hope with realistic expectations for recovery is important. People need encouragement to seek professional help such as that offered by the Red Cross Access to Care program, Speier states. And they need a reliable recovery timeline, along with simultaneous return of schools, hospitals and a justice system so that they can more confidently invest in re-establishing themselves. "It's important for people to know that time is critical," Redlener says. "Most adults will be okay once they have homes and can return to normalcy. But thousands of children at critical developmental ages will now have been rootless for upward of two years, with yet incalculable consequences."

LINGUISTICS

Speaking in Tones

Ni hao or bonjour: do genes drive preference for language type? **BY CHARLES Q. CHOI**

Just as humans are different genetically, so are they diverse linguistically, speaking at least 6,800 known tongues worldwide. New findings suggest genetics could explain some of the variety seen in language by, at times, leading to preferences for tones. The means by which this link works remains unclear, and some researchers dispute whether it exists.

For the most part, languages are either unambiguously tonal or not. In tone languages, such as Mandarin in China or Yoruba in West Africa, the pitch of a spoken word affects its meaning. For instance, in Mandarin, *ma* said in a high, level tone means "mother" but in a low, rising tone means "horse." In English, a word's pitch



DO-RE-MI: The right pitch is essential in tone languages, because it will affect a spoken word's meaning.

conveys emotion but often does not influence meaning. (Notable exceptions to this dichotomy include Japanese, where words can differ depending on the pitch of syllables—technically, *moras*—within them.)

This distinction could be genetic, propose University of Edinburgh linguists Robert Ladd and Dan Dediu. The pair analyzed DNA sequences from public databases to investigate two genes linked with brain growth and development, *ASPM* and *Microcephalin*. They wanted to see how these genes correlated with 26 linguistic features, such as number of consonants, and how they varied among 49 distinct populations in the Old World.

The researchers discovered that people

who carried recently evolved forms of the genes tended to speak nontonal languages, with the newer versions of *ASPM* and *Microcephalin* appearing roughly 5,800 and 37,000 years ago, respectively. Prior studies showed that these mutations apparently do not affect intelligence, brain size or sociability. Ladd and Dediu instead suggest in the June 26 *Proceedings of the National Academy of Sciences USA* that these mutations lead to subtle differences in the cerebral cortex related to language and tone.

Ladd emphasized that there are no “genes for Chinese.” As he explains it: “If you raised a boy from China in Kansas, you wouldn’t find him speaking Chinese, and vice versa.” Still, people might take slightly different routes to learning certain languages because of their genes. “It may even be that some find it easier to acquire tone languages than others,” he adds.

Others argue that no genetic predisposition for tone languages exists. Perceptual and cognitive psychologist Diana Deutsch

of the University of California, San Diego, has found that speakers of tone languages are more likely to have perfect pitch—the ability to identify any pitch heard without hearing a reference note. Her work also hints that perfect pitch is not rooted in genes—and, by extension, tone languages are not, either. Deutsch adds that the apparent link Ladd and Dediu saw “could just be a coincidence” that further research would undo, something Ladd agrees with.

Still, although perfect pitch and tone



BUT DOES IT SOUND RIGHT? A study concludes that a genetic predisposition may exist for tone languages, such as Chinese, over non-tone tongues, such as English.

languages appear linked, “that doesn’t mean that perfect pitch is necessary for tone languages,” remarks Northwestern University neuroscientist Patrick Wong. Instead he suggests that if *ASPM* and *Microcephalin* do play a role with tone languages, the genes might help in hearing high and low pitches, incorporating high or low pitch into words and sentences or tracking patterns in changes of pitch. Wong finds Ladd and Dediu’s work “very interesting” but “inconclusive.”

Ladd notes that future studies could focus on people as they seek to learn new tone languages and see whether any mutations of *ASPM* and *Microcephalin* are linked with their level of success. Still, he thinks that even if the genes do play a role in tone and language, “these could be very subtle effects that simply do not get noticed against a background of other factors related to a person’s upbringing.”

Charles Q. Choi is a frequent contributor.

RANDY FARIS Corbis

SECURITY

Muons for Peace

New way to spot hidden nukes gets ready to debut **BY MARK WOLVERTON**

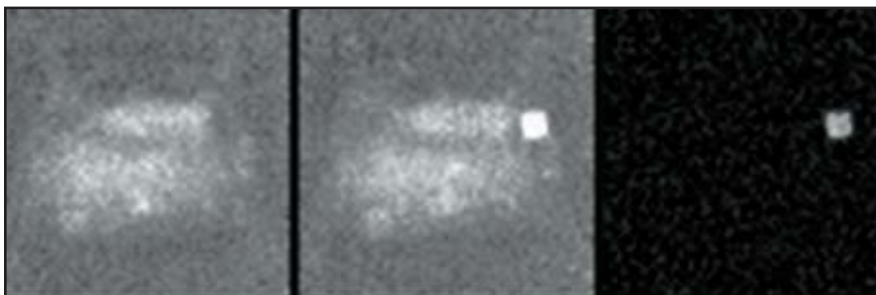
The same place that gave the world the atomic bomb has now found a way to ferret out illicit nuclear material. Los Alamos National Laboratory has developed a method to search for heavy elements such as uranium via subatomic particles from space called muons. By 2008, “muon tomography” might be guarding U.S. borders.

About 10,000 muons reach every square meter of the earth’s surface a minute; these charged particles form as by-products of cosmic rays colliding with molecules in the upper atmosphere. Traveling at relativistic speeds, muons can penetrate tens of meters into rocks and other matter before attenuating as a result of absorption or deflection by other atoms. The scattering is most pronounced in dense substances such as uranium and plutonium—elements with

high *Z* (the number of protons in an atom’s nucleus). “We use the fact that the scattering is sensitive to *Z* and particularly sensitive to the materials that you build nuclear bombs from or that you shield nuclear bombs with,” explains Los Alamos’s Christopher Morris, chief creator of the

technology. “We measure the scattering angle for every muon, we measure the angle on the way in and the angle on the way out, and the change in the angle tells you how much material you’ve gone through.”

After 9/11 heightened security concerns, Morris and his team realized that



MUON VISION: An automobile engine (left) is imaged based on the muons that pass through it. The scan reveals a lead cube hidden inside the engine (center). The lead becomes plainly visible when the muon data for the engine are subtracted (right).

CHRISTOPHER MORRIS Los Alamos National Laboratory

Subatomic Help for Subterranean Threat

Physicist Luis Alvarez was the first to use muons to peer inside objects, as he searched for hidden chambers inside one of the Giza pyramids in the 1960s. He did not find any, but his work proved the viability of muon radiography. Besides guarding against terrorism, muons could warn of natural threats. Hiroyuki Tanaka of the University of Tokyo and Toshiyuki Nakano of Nagoya University in Japan have used special photographic plates to collect muons passing through Japan's volcanic Mount Asamayama. Changes in the number and direction of muons provided images of the volcano's interior and the movement of magma within, raising the possibility that the technique could predict imminent eruptions.



muons could provide a way to detect smuggled nuclear materials better than existing x-ray, neutron, or gamma probes, which can expose people to stray radiation. That is not a problem with muon scanning, because muons are already naturally present. And whereas shielding can defeat other scans, it only makes nuclear contraband easier to find with muons: the dense shielding stands out prominently with muon tomography, which lacks the background scatter that blurs x-ray images.

A prototype muon tracker, completed in 2006, successfully sniffed out test objects such as a 10-centimeter cube of lead hidden inside an engine block, something that would have evaded a conventional x-ray scan. "It gave us the confidence that this technology would definitely work and that we were ready

to move on to the next stage of development," says Erica Sullivan, Los Alamos's technology transfer liaison.

Decision Sciences Corporation, a San Diego-based software company specializing in defense applications, discovered the Los Alamos work and became even more enthusiastic on learning that muon tomography could also spot medium-Z bomb-making ingredients, such as iron and copper, which are used in improvised explosive devices. That led to a formal agreement this past spring between Los Alamos and Decision Sciences to develop a commercial muon tomography system for homeland security use.

The partnership is now busy constructing an operational prototype. "This is no longer laboratory simulation or physics simulation or small scale, this is now the real thing in real size," says Dave Klugh, Decision Science's manager for the effort. A commercial version of the scanner,

dubbed Guardian MT, is expected by 2008.

Unlike the lab-size prototype, the commercial muon tomography scanner will be a tunnel big enough to drive a semitrailer truck through. Layers of aluminum detector tubes will enclose a volume of about 16 feet high by 12 to 14 feet wide, for about a length of 60 feet. Each gas-filled tube will have a thin wire running down its middle to detect muons by the telltale ionization trails left when they have passed through. Scanning times for detailed, tomographic pictures can vary from 20 seconds up to a minute, depending on the size and loading of the vehicle. As the system "learns" the configuration of various vehicle makes and models, it can ignore known innocuous data such as the engine and transmission, cutting down the scanning time—and making anything unusual stand out even more.

Donald Geesaman, senior physicist and acting associate director of the phys-



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ics division at Argonne National Laboratory, calls the Los Alamos project “very intriguing.” He notes that the team members “have made significant progress in the difficult problem of obtaining suffi-

cient imaging resolution for this purpose.”

With major funding now coming from Decision Sciences, the developers are confident that by next year, muon tomography will be up and running. As Klugh sees

it: “There is a definite need for this type of product, and the need existed yesterday.”

Mark Wolverton writes about science and technology from Bryn Mawr, Pa.

NERVE REGENERATION

Healing Broken Nerves

Combination therapy as the best approach for damaged spinal cords **BY ANNA GRIFFITH**

Ever since the 1940s, when researchers discovered that nerves of the spinal column can grow, scientists have tried to devise ways to coax the cells to overcome damaged areas and thereby defeat paralysis, organ degeneration and other problems associated with injury to the central nervous system. Removing scar tissue with drugs, laying down scaffolds and inserting cells have all been tried with varying degrees of success. Recent achievements, such as the restoration of some ability to walk in rodents, and other findings indicate that rather than a single approach, all may be the key. “A combination of drugs and cells gives better results than just any one of the components on their own,” says Naomi Kleitman, a program director at the National Institutes of Health’s National Institute of Neurological Disorders and Stroke.

Injury to nerves produces inflammation, ion imbalance, scar tissue and cysts filled with cerebrospinal fluid, which damage additional neurons and create a barrier against neuron growth. A lesion just one millimeter wide can increase to five to 10 millimeters, too large a gap for neurons to bridge. Surviving neurons often lose myelin, the insulation needed for reliable and quick signal transmission. About 200,000 people in the U.S. live with spinal cord injury.

Several compounds now in phase 1 clinical testing may counteract growth-blocking elements. BioAxone Therapeutic in Quebec found that 30 percent of patients improved after receiving Cethrin, a drug thought to counteract inhibition.

Novartis has ATI-355, an antibody against the inhibitory protein Nogo. Researchers have shown in preclinical tests that an enzyme isolated from bacte-

ria, chondroitinase, dissolves scar tissue.

Besides removing inhibition, scientists are promoting the growth of new neurons. Until five years ago, they could not control

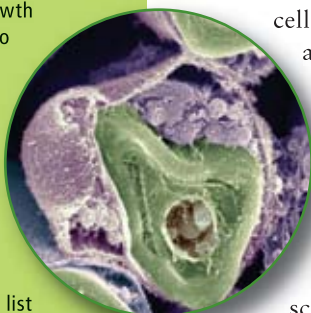


LOOKING TO RECONNECT: A combination of approaches seems essential to repair damaged tissue of the central nervous system. This x-ray of a neck fracture shows a complete spinal cord tear between cervical vertebrae five and six.

SCOTT CAMAZINE/Phototake

Cellular Connections

When it comes to replacement tissue for spinal cord repair, stem cells have taken center stage. But other cell types might also mend broken nerves and have shown promise in animal studies. For instance, transplanted glial Schwann cells (*photograph*) provide a natural source of myelin (green) and neurotrophic growth factors. Patients have gone to China and Portugal for an injection of olfactory-ensheathing cells, and some have reported partial restoration of feeling and movement. Such experimental procedures (many not available in the U.S.) have yet to prove themselves in actual clinical trials, however. A full list of the types of cells that might repair injured central nerves can be found in an experimental treatments report from the International Collaboration on Repair Discoveries (www.icord.org/iccp.html).



western University, has designed peptides that self-assemble into nanofibers many thousandths the size of a human hair. The prevalence of a specific sequence of amino acids, dubbed IKVAV (for isoleucine, lysine, valine, alanine and valine), on the outer surfaces of the scaffold promotes neuron growth.

In rats, the scaffold trapped stem cells, signaled them to replicate and guided their differentiation into neurons while suppressing the formation of scar-forming glial cells. Scientists at the Massachusetts Institute of Technology and Hong Kong University used a similar peptide scaffolding to restore vision to surgically blinded hamsters. Such therapies may also be adapted to treat stroke and neurodegenerative disorders.

Research by neurologist Douglas Kerr

of Johns Hopkins University shows the benefit of combining treatments. His team used stem cells, drugs to remove scar tissue, and a combination of growth factors and signaling cues to re-create an environment reminiscent of early nervous system development. Animals receiving treatments missing just one component of the cocktail showed no sign of recovery. Kerr and his colleagues are testing human embryonic stem cells in pigs and will continue doing so for several years before seeking approval for human trials. Combined treatment studies “are the most important of them all,” Guth says, and worth the effort to determine precise dosage, timing and combination of drugs to avoid harmful interactions.

There is still a long way to go. Many studies have restored paralyzed rats’ ability to walk, but Guth notes that rats (and cats) can walk nicely with just 5 to 10 percent of their spinal cord intact. And if the spinal cord is severed early in life, before

the fate of stem cells. Now, using proteins and other chemicals that guide nervous system development and trigger cell differentiation, such as retinoic acid and sonic hedgehog protein, they can direct stem cells to secrete growth factors or to become essential neural components: spinal motor neurons for treating paralysis, myelin-producing oligodendrocytes for multiple sclerosis, or dopamine-producing cells for Parkinson’s. Pending safety studies, Geron, a biotechnology company in Menlo Park, Calif., plans to file for FDA approval of human stem cell trials later this year. “Perhaps stem cells are the breakthrough we’re looking for,” says nerve regeneration pioneer Lloyd Guth, who retired from the University of California, Irvine, and now lives in Williamsburg, Va.

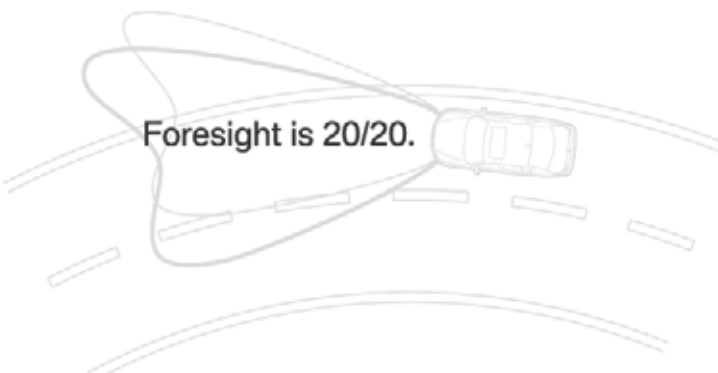
The final “connector” could be biological scaffolding. These structures would orchestrate the actions of various cells and growth factors while creating a physical bridge for the exquisitely complex and precise process of regenerating the central nervous system. Samuel Stupp, director of the Institute for Bio-Nanotechnology in Medicine at North-

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inhibitory connections are made, the animals retain the simple reflex of walking. They can walk even though they lack substantial input from the brain—"like a chicken with its head cut off," Guth says, a feat he doubts humans could replicate.

Motor and sensory pathways may need their own treatments. Besides requiring different growth factors, motor fibers may just need to regrow far enough to connect

with a neural network within the spinal cord responsible for walking reflexes, whereas sensory fibers may need to travel all the way to the brain, Kleitman notes.

Clinical treatment should proceed with caution. Natural growth inhibition after injury occurs to protect against harmful rewiring, and patients in a few clinical studies now have pain because regenerating neurons grew the wrong way. Predict-

ing a cure for paralysis is unfair to the public, Guth says: "A breakthrough, by definition, is an unanticipated event; however, because of the recent tremendous activity in the field, we have to be optimistic that a breakthrough will happen."

Anna Griffith is based in Chico, Calif. She described progress in "brain chips" for memory in the February issue.

DIGITAL RIGHTS

Déjà Vu Disks

For Blu-ray and HD DVD, encryption and court orders prove futile—again **BY SOURISH BASU**

In the never-ending cat-and-mouse game between digital media distributors and enthusiastic code breakers, the latter seem to have gained the upper hand when it comes to HD DVD and Blu-ray disks. Already twice this year amateur programmers have released keys for these next-generation DVDs, enabling playback and copying via unlicensed devices. The inability of copyright authorities to stay ahead—by issuing either new keys or cease-and-desist orders—prompts the question of whether such policies are the best way to balance fair use with intellectual-property rights.

When DVDs came out in the mid-1990s, the entertainment industry tried to protect their content from piracy through an encryption scheme called the content scrambling system (CSS). Playback devices needed a 40-bit key to unlock the encrypted files. In 1999 hackers exploited a cryptographic weakness of CSS and created a program called DeCSS, which enabled unlicensed machines to play DVDs. As cryptographer Bruce Schneier, founder of the security consultants BT Counterpane, once remarked, making digital files impossible to copy is about as easy as making water not wet. So copy protection fell to the passage of laws such as the Digital Millennium Copyright Act, passed in the U.S. in 1998, which makes circumventing access-control measures on digital media illegal.



CREATIVE LICENSE: Responding to legal efforts to keep leaked digital keys secret, people have expressed the keys through various means on public Web sites, such as this image posted on the photograph-sharing site Flickr, showing one key.

Resulting legal actions banned the dissemination of DeCSS, sparking widespread civil disobedience. Activists expressed the DeCSS code and key in various creative ways, including on

T-shirts, as tattoos, through a haiku and even as a single prime number (which therefore earned the dubious distinction of being the first illegal number). Eventually CSS authorities dropped the last of

their CSS-related lawsuits in 2004.

The HD DVD and Blu-ray disks, apart from offering at least three times the storage capacity of standard DVDs and a higher video resolution, use a much stronger encryption called the advanced access content system (AACS). Not only is the underlying cipher stronger (128 bits), but each disk player also has a unique set of keys. If someone hacks a player and deciphers a key, content providers can revoke the compromised player by reengineering newer disks to be playable on all devices except that one. This capability differs markedly from CSS, where a single leaked key renders the entire scheme void.

This past January crypto enthusiasts broke through AACS's layers of security and published a numeric processing key in an online forum. Lawyers representing the AACS Licensing Authority, an oversight consortium founded by Disney, Microsoft and six other corporations, sent cease-and-desist letters to Web-feed aggregator sites, directing them to remove posts containing the key, which thus became another illegal number.

After one such site, Digg, complied, its users rebelled. Reminiscent of DeCSS days, people made songs, haikus and music videos with the number and spread it throughout cyberspace. Eventually the licensing authority revoked the compromised key and issued a new one. But then, another diligent code breaker discovered the revised processing key in late May, possibly sending the consortium back to square one. Proskauer Rose, the law firm representing the consortium, refused to comment on the issue.

Noting the futility of access-control measures for digital material—even Microsoft security engineers have acknowledged this problem in a 2002 analysis popularly called the Darknet Report—content providers seem to be considering other approaches. At the 2007 Consumer Electronics Show, Disney chief executive Robert Iger remarked that “the best way to combat piracy is to bring content to market on a well-timed, well-priced

Act of Suppression

The Digital Millennium Copyright Act of 1998 bans circumventing access-control measures on digital media. It makes fewer exceptions for fair use than existing U.S. copyright laws, and as White House cybersecurity chief Richard Clarke remarked in 2002, license holders have used the act to suppress legitimate computer security research. For example, a multi-industry group called Secure Digital Music Initiative (SDMI) threatened legal action against Princeton University cryptographer Edward Felten to prevent disclosure of vulnerabilities in its watermarking scheme for digital music, which he broke in response to SDMI's public challenge to do precisely that.



basis,” which would make media piracy less lucrative, if not irrelevant. The Electronic Frontier Foundation (EFF), a non-profit organization dedicated to digital freedoms, has, on the other hand, been recommending a collective licensing scheme for years. Such a scheme would resemble the one used by radio stations, which pay a blanket fee that is redistributed among artists given airtime.

But content providers may still prefer to play cat and mouse. “Copy-protection technologies do not have to work to be useful to the entertainment industry,” says EFF copyright lawyer Fred von Lohmann.

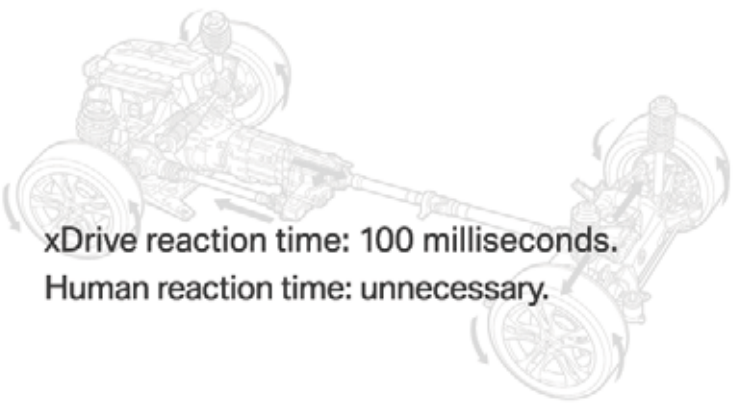
The real benefit of such technologies to the industry, he adds, is that they provide the industry with “the means to control the nature and pace of innovations and eliminate the capacity of disruptive technologies [such as DeCSS and unlicensed players] to undermine its business model.”

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ASTRONOMY

Dangling a COROT

Space telescope aims to find more planets orbiting other stars **BY ALEXANDER HELLEMANS**

This year is shaping up to be an important one in the search for planets around other stars. In April astronomers at the Geneva Observatory announced the discovery of the most Earth-like exoplanet yet located, the first rocky world beyond our solar system that could hold liquid water. Just 1.5 times the size of Earth and possessing five times its mass, the planet circles the red dwarf Gliese 581. More such announcements will likely come in the months to follow, as the first space observatory dedicated to hunting exoplanets, called COROT, begins full operation and researchers complete their calculations.

In hunting for other worlds, scientists have proved adept at wringing the most from ground-based observatories. The Geneva astronomers found the rocky, Earth-like planet by first detecting the slight wobbling in the motion of its parent star, as star and planet circled around their common center of gravity. Such wobbling betrays itself as tiny Doppler shifts in the spectral lines present in a star's light. Although the investigators determined the exoplanet's mass via the observed movement, they could not directly gauge its size, because it does not transit—that is, pass in between Earth and its parent star. Hence, the team had to derive the exoplanet's density from planet formation models, team member Stéphane Udry reports.

Even if the planet moved across its star, the team might not have been able to see it. Peering through Earth's turbulent atmosphere requires adaptive optics to correct for distortions, but the same technology also precludes precise measurements of the dimming of light when a planet passes in front of a star. Even with future giant telescopes up to 42 meters in diameter, the sen-

sitivity for such photometric detection will remain limited. "It is difficult to combine transit search with adaptive optics," Udry explains. "Adaptive optics continuously disturbs the photometric calibration."

That is where space observatories come in, such as the \$46-million COROT (CONvection ROTation and planetary Transits). In addition to studying the ripples on the surface of stars to glean information about their interior, the observatory looks at changes in stellar luminosity that might indicate an exoplanetary transit.

COROT began taking

MASS TRANSIT: The COROT satellite will look for exoplanets that transit, or pass in front of, their parent stars.

measurements in February, and, once fully calibrated, its 27-centimeter-wide telescope will detect light variations as low as one part in 20,000—200 times the resolution of ground-based instruments. COROT will ultimately look at 120,000 stars. "It is a hit-or-miss search, but we need a large number of stars so as to increase the probability of discovering planets," explains Pierre Barge of the Astrophysics Laboratory of Marseille in France, who leads the COROT exoplanet working group.

Besides finding exoplanets, COROT will also be able to determine their sizes, because the amount of dimming during a planet's occultation is proportional to that planet's girth. Moreover, knowing its size pins down its density and hence confirms whether the planet is rocky or gaseous.

Currently, astronomers know the diameter of only about 20 of the approximately 240 known exoplanets.

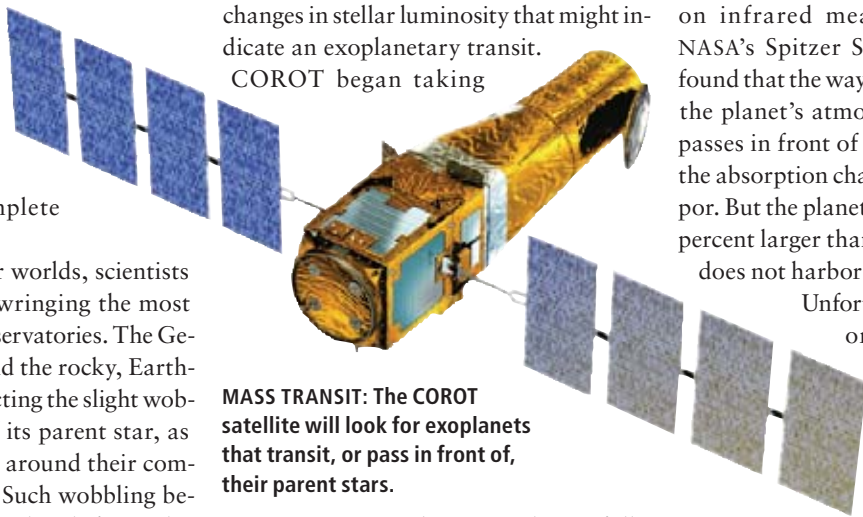
Other space observatories can use transits to discover details about any atmosphere that might enshroud an exoplanet. In the July 12 *Nature*, Giovanna Tinetti of the European Space Agency and University College London and her colleagues report the discovery of water on a planet circling a star 64 light-years away, based on infrared measurements taken by NASA's Spitzer Space Telescope. They found that the way the light is absorbed by the planet's atmosphere when the body passes in front of its parent star matches the absorption characteristics of water vapor. But the planet is a gas giant, about 15 percent larger than Jupiter, so it probably does not harbor life.

Unfortunately, none of today's orbiting observatories, not even the Hubble Space Telescope, can find water on smaller worlds. "They are not sensitive enough to go for the smaller rocky

planets," Tinetti says. She expects that such detections will come within the reach of the James Webb Space Telescope, Hubble's successor, which will be launched in 2013.

Space observatories will not put their terrestrial counterparts out of business in the search for exoplanets. Ground instruments can detect Doppler shifting quite well and are needed to corroborate findings from space. COROT has already spied possible new exoplanets, but researchers will not announce results until later this year. "We have to do a certain number of checks," Barge says. If the checks pan out, expect to hear a lot more otherworldly news.

Alexander Hellemans is a science writer based in Antwerp, Belgium.



Data Points

Green Burning Man

Black Rock City—complete with a post office and volunteer emergency service crews—rises from Nevada's Black Rock Desert for only one week of every year, thanks to Burning Man, a festival of art and counterculture. Running from August 27 to September 3, it ends with the destruction of the "city," capped by the arsonous elimination of art, structures and a central effigy of "the man." This year's event, dubbed Green Man, has an environmental theme. Organizers will try to offset the carbon footprint of the festival. They will decrease solid waste by 70 percent through composting and shredding and switch from last year's 20,000 gallons of

diesel to 20,000

gallons of

local biofuel

derived from cooking

grease and supplied by Bently Bio-

fuels in Minden, Nev.

They will also deploy a

30-kilowatt solar array

for the event and partner

to build a 150-kilowatt

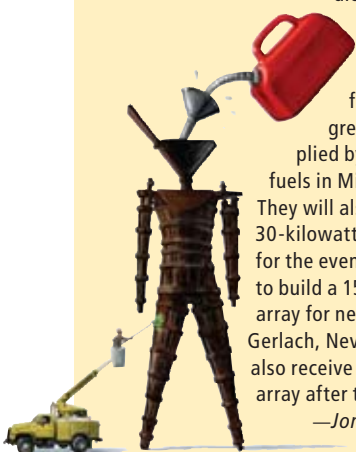
array for neighboring

Gerlach, Nev., which will

also receive the smaller

array after the event.

—Jonathan Scheff



Burning Man attendees: **40,000**

Carbon emissions from burning
"the man": **112 tons**

Total on-site emissions:
2,473 tons

Emissions from participants' travel:
25,019 tons

Weeklong carbon offset by the
30-kilowatt solar array: **6.9 tons**

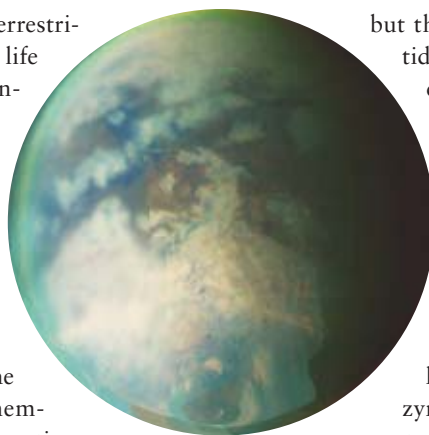
Annual carbon offset by the
30- and 150-kilowatt arrays:
559 tons

SOURCES: Tom Price, Burning Man staff; David Shearer and Jeff Cole, founders of the CoolingMan Project

EXO BIOLOGY

Life Not as We Know It

The search for extraterrestrials must look beyond life as we know it, scientists have advised NASA. The space agency mostly hunts for life that, like on Earth, is based on water, carbon and DNA, a National Research Council committee found. The dozen committee members—specialists in genetics, chemistry, biology and other fields—instead recommend NASA consider what they call "bizarre life." For instance, synthetic biology experiments have devised molecules that encode genetic data



but that have more nucleotides than DNA or RNA do. Instead of water, aliens might employ ammonia or sulfuric acid as the basis for their life-sustaining biochemical reactions. Novel organisms might use minerals as catalysts, rather than enzymes. In their July 6 report, the council scientists singled out Saturn's moon Titan (*photograph*) as especially deserving of a follow-up mission because of evidence of mixtures of liquid ammonia and water in its interior.

—Charles Q. Choi

EVOLUTION

Ulcers from the Deep

Genes that help harmful germs thrive in the warmth of the human body apparently arose from DNA that enables microbes to survive in superheated deep-sea vents. Scientists at the Japan Agency for Marine-Earth Science and Technology compared the genomes of two deep-sea bacteria with those of *Helicobacter*, responsible for ulcers, and *Campylobacter*, the leading food-borne cause of diarrhea. According to the researchers, genes that likely help deep-sea bacteria maintain symbiotic relationships with other vent-dwelling organisms assist their gut-dwelling relatives in evading immune systems. Enzymes that help vent microbes live off hydrogen enable *Helicobacter* and *Campylobacter* to do the same in the digestive system. And like their harmful kin, deep-sea bacteria have few DNA repair genes, allowing frequent mutations to occur and enabling the microbes to adapt quickly to changing conditions or to resist immune responses. The researchers suggest the human-harming bugs evolved from deep-sea ancestors and later acquired more virulence factors while living in symbiosis with animals. The *Proceedings of the National Academy of Sciences USA* published the findings July 17.

—Charles Q. Choi



HOT ZONE: Genes that help bacteria live in hydrothermal vents also help *Helicobacter* (*inset*) live in human stomachs.

MATT COLLINS (illustration); NASA/JPL/UNIVERSITY OF ARIZONA (Titan); B. MURTON/Southampton Oceanography Center/Photo Researchers, Inc. (sealife); GARY GAUGLER/Photo Researchers, Inc. (Helicobacter)

In Brief

SUPERCONDUCTING AIRPLANES?

Superconductivity may be the key to electric jet engines for lowering greenhouse gas emissions from aircraft, which contributed 9 percent of the total U.S. greenhouse gas emission in 2003. A study out of Florida A&M and Florida State Universities finds that, for small planes, superconducting turbines would be lightweight and powerful enough to run on electricity from clean-burning hydrogen fuel cells. The liquid hydrogen could also chill the superconductors. But the savings would come at the steep premium of \$2 million just for a prototype. —JR Minkel

STEM CELL VETO—AGAIN

On June 20, President George W. Bush for the second time vetoed legislation that would have lifted limits on federally funded research on embryonic stem cells. Congressional advocates tried to muster the votes to override the veto but fell short of the two-thirds majority needed. The measure would have allowed research only on cells extracted from unused embryos at fertility clinics that donors chose to give rather than discard. Ironically, the veto came the same day as a *Science* report that found that 60 percent of patients with surplus embryos in U.S. fertility clinics would likely donate them to create stem cell batches or lines for research; only 22 percent said they would hand them over to other infertile couples. —Lisa Stein

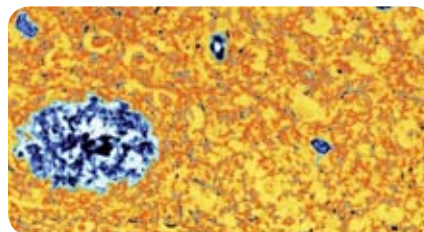
OPENING THE DOOR TO HIV

The mutation that enabled humans to fend off an ancient monkey virus appears to have made us more vulnerable to HIV-1. Virologists at the Fred Hutchinson Cancer Research Center in Seattle studied the immune protein TRIM5-alpha, which protects rhesus monkeys but not humans from HIV-1. They found that the human version of TRIM5-alpha protected cells against a resurrected portion of the extinct primate retrovirus PtERV1, suggesting that it evolved to fend off the virus. In proving itself against PtERV1, however, the human TRIM5-alpha lost the ability to fight HIV-1, the scientists say in the June 22 *Science*. —JR Minkel

MOLECULAR BIOLOGY

Prions against Alzheimer's

Misshapen proteins called prions lie at the root of mad cow disease and similar brain ailments, but the role of these molecules in their normal form remains unclear. In humans, normal prion proteins may generally protect against Alzheimer's disease. In Alzheimer's, abnormally folded beta-amyloid protein accumulates in the brain. Biochemist Nigel Hooper of the University of Leeds in England and his colleagues found that high levels of normal prion proteins in human cells prevent beta-amyloid formation by inhibiting an enzyme called beta-secretase. The brains of mice genetically modified to lack normal prion proteins had significantly higher beta-amyloid levels. Hooper says that prion proteins might prevent Alzheimer's



AMYLOID PLAQUE of Alzheimer's disease could be fended off by prion proteins.

Alzheimer's from occurring earlier than it usually does in life or that perhaps they guard against oxidative stress, which has been linked to Alzheimer's and other neurodegenerative diseases. Further research could lead to new drugs that target beta-secretase, he adds. The team reports its findings in the June 26 *Proceedings of the National Academy of Sciences USA*.

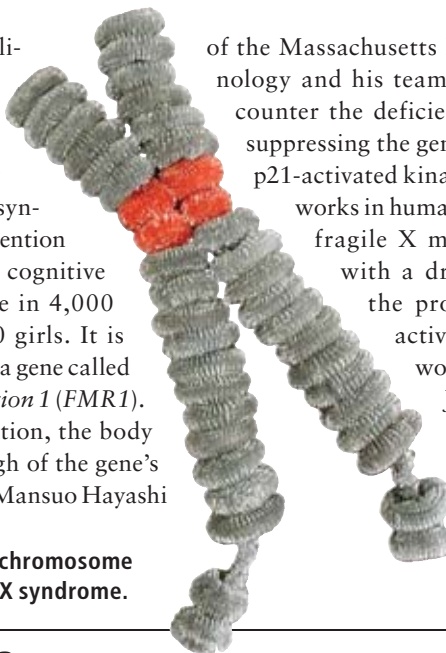
—Charles Q. Choi

GENETICS

Developmental Disorder in Mice Reversed

A developmental disability caused by a mutated gene on the X chromosome can be reversed by a second mutation, at least in mice. Fragile X syndrome, which causes attention deficiency, anxiety and cognitive dissonance, affects one in 4,000 boys and one in 6,000 girls. It is caused by a mutation of a gene called *fragile X mental retardation 1* (FMR1). As a result of this mutation, the body does not produce enough of the gene's corresponding protein. Mansuo Hayashi

of the Massachusetts Institute of Technology and his team found a way to counter the deficiency—namely, by suppressing the gene for the enzyme p21-activated kinase. If this process works in humans, then reversing fragile X might be possible with a drug that inhibits the production of p21-activated kinase. The work appears in the July 3 *Proceedings of the National Academy of Sciences USA*. —Nikhil Swaminathan



FRAGILE SITES: Ends of X chromosome show damage in fragile X syndrome.

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SciAm Perspectives

Take Nutrition Claims with a Grain of Salt

Dietary studies sponsored by the food industry are often biased

BY THE EDITORS

Although we are what we eat, we are by no means *only* what we eat. Some people, for instance, can consume all the fatty foods they want—meat, cheese, butter, ice cream—but somehow manage to stay rail-thin and enjoy low blood triglyceride levels, whereas others living on the same rich fare would soon develop potbellies and clogged arteries. The significant genetic and metabolic variation among individuals makes it almost impossible for experts to prescribe detailed nutritional recommendations that work optimally for everybody. As nutritionist Marion Nestle recommends in her article “Eating Made Simple,” beginning on page 60, the best we can do today is to adhere to the time-honored advice to eat less; exercise more; eat mostly fruits, vegetables and grains; and avoid junk foods.

But this basic regimen leaves many concerned Americans with unresolved issues about dietary choices, especially those regarding specific foods

promoted by food companies and their lobbyists: Is milk bad for adults? Should I eat more fish? Are organic foods better? More specific guidance regarding food selection would help.

Regrettably, determining the actual health value of organics, fish, milk or any other single foodstuff or nutrient is no easy task, nor is it cheap. The complexity of nutrition and its subtle effects on human well-being mean that researchers must mount large, long-term studies to try to distinguish among multiple, interrelated nutritional factors that affect health. But big test group populations are costly to monitor accurately and difficult to control over time.

Despite the complexities, such large-scale nutrition-related studies are important because they help to shape how government and professional authorities formulate dietary guidelines, how administrators design public health programs and how agencies regulate company health claims for food products. The popular media publicize these findings widely, which directly affects consumer behavior. More and more, the commercial success of food products depends on what science says about the effects of these foods on health. Yet all too often the sources of the science are the commercial interests themselves.

Although government

agencies as well as some charities and activist groups sponsor major nutrition experiments in the public's interest, these organizations often lack sufficient resources to conduct the research that might more fully inform people about what to eat. Given the chance to gain favorable, peer-reviewed publicity for their products, food companies frequently fill the research-study funding gap and then vigorously promote any results that support consuming a specified daily amount of one of their foods.

Unfortunately, food industry money seems to distort nutrition studies, according to the first systematic effort to measure sponsorship bias in nutritional research. That analysis appeared in a paper published this past January in the *Public Library of Science Medicine*. A research team at Children's Hospital Boston performed a meta-analysis of 206 nutrition-related studies on milk, juice and soft drinks conducted from 1999 to 2003. Of the 111 that had declared financial sponsorship, 54 percent were at least partly funded by industry. Industry-supported studies were four to seven times more likely to favor their sponsors than research paid for by disinterested parties.

The influence of sponsors may be unconscious, the investigators suggest, and could occur at many levels, manifested by how researchers pose questions in the hypothesis, how they design studies, which data they collect or do not collect, how they analyze the data and how they derive their conclusions.

Critics have also noted that the Chil-



THE EDITORS' BLOG

Posts from SciAm Observations, see www.SciAm.com/blog

Raiders of the Lost Beech Veneer

Posted by Gary Stix, July 6, 2007

According to Wikipedia, IKEA purports to be a "pioneering force in sustainable approaches to mass consumer culture." Once construction of its store in Nanjing, China, is finished, consumers there will be able to share, along with the rest of the globalized world, the experience of puzzling over hieroglyphic assembly instructions supplied by the McDonald's of modular assembly.

While joining the "sustainable" mass consumer culture, they will miss the chance to enjoy a piece of their own culture. In constructing the Nanjing store, the workers destroyed about 10 ancient tombs that date back 1,800 years and encompass six dynasties, notes a report in a city newspaper that was picked up by Reuters.

In their place, the citizens of Nanjing will now be able to line up for a Ramberg three-door wardrobe or Aneboda drawers that you can be certain will last another 2,000 years.

Bat Flu

Posted by Christopher Mims, June 28, 2007

You're sitting at home watching television, when suddenly a bat flies in the open door of your home, flutters about frantically for a few minutes, then leaves. Days later you develop a high fever and acute respiratory illness—a week after that your children are sick, too.

Such was the predicament of a Malaysian man who appears to be the first ever recorded case of a bat-to-human transmission of a bat virus—frightening stuff, given that bats can carry the SARS, Nipah and Hendra viruses.

Dubbed "Melaka" by its discoverer, Linfa Wang of the Australian Commonwealth Scientific and Research Organization, the respiratory infection causes a severe reaction in humans but is not lethal. It does appear, however, to possess the one trait that experts fear will arise in bird flu—Melaka is transmissible between humans.

Wang's results appear in the July 3 issue of the *Proceedings of the National Academy of Sciences USA*.

dren's Hospital group may have distorted the study's findings by failing to include in their analysis nutrition research funded by the U.S. Department of Agriculture (presumably the critics believe that government-supported investigations are more likely to be free of industry influence).

The realization that all organizations—including the government, as well as industry and activist groups—tend to finance research that is aligned with their

interests seems to lead to a straightforward solution. Because nutrition research is important to helping the public make healthy food choices, it only makes sense to find public monies with which to support the independent studies needed to develop the necessary guidelines. People, we think, are likely to deem it worthwhile to pay a bit to find out whatever science can legitimately say about what to eat. ■

Sustainable Developments

Breaking the Poverty Trap

Targeted investments can trump a region's geographic disadvantages

BY JEFFREY D. SACHS



The most destitute regions of the planet—in Africa, Central Asia, the Andes and a few other places—are not merely poor: they are seemingly trapped in poverty and prone to internal violence and political collapse. The regional distribution of these poverty traps is not random. None are in Europe or North America. Asia now has only a few. Most of tropical Africa is in a poverty trap or barely emerging from one, but northern Africa and South Africa are not.

What can we learn from these geographic patterns?

As noted in previous columns, the primary problem in most impoverished places is low food productivity, typically as a result of dependence on irregular rainfall rather than irrigation; on weak and easily weathered soils; and often on steeply mountainous, degraded land. The second problem is a heavy burden of

disease. The tropics, especially in Africa, are home to lethal and debilitating diseases that are nonexistent or easily controlled in temperate zones. Malnutrition also raises the disease burden markedly. The third obstacle is physical isolation. Many impoverished states are landlocked, with no easy access to sea-based trade. And even countries with seaports can face extreme transport problems because of mountainous terrain, large inland populations and overall remoteness from world trade routes.

These problems, rooted in geography, set the poverty traps. Food insecurity leads to malnutrition, sickness, hunger-induced violence, and zero- or low-cash incomes for farm households, which are stuck without the means or creditworthiness to invest in agricultural improvements. The poor may have to "mine" the local environment unsustainably by depleting the soil, overfishing, overhunting and cutting down forests. They are in-

Africa is primed for a green revolution breakthrough.

creasingly affected by climate change.

The political consequences are equally stark. In his book *States, Scarcity, and Civil Strife in the Developing World* (Princeton University Press, 2006), political scientist Colin H. Kahl of the University of Minnesota describes two main paths by which extreme poverty raises the likelihood of violent conflict and the collapse of a state into lawlessness. First, when deepening poverty leaves the population desperate and the government unable to respond, groups may "self help" by fighting for resources with other groups. Somalia has experienced such a collapse in the past 20 years. Alternatively, if a government takes sides, it may use the state apparatus, even violently, to favor one group against another. The Rwandan genocide was such a phenomenon.

Geographic factors do not change easily. Yet programs of targeted investments by outside sources can break poverty traps at surprisingly low cost. Begin by focusing investments on raising food security and agriculture productivity; enable

farmers to gain access to fertilizers, high-yield seeds, small-scale water management technologies and improved livestock management. The result can be a rapid boost in food production and farm incomes, commonly called a green revolution. Africa is primed for such a breakthrough, if donors support it.

The tropical diseases, especially malaria, worm infections and many other water-borne and insect-borne diseases, are readily preventable and often completely treatable. What is needed is a supply chain of crucial commodities, the construction and availability of primary health units in rural areas, and trained village health workers. The results can be dramatic, with a sharp drop in child mortality and a rapid

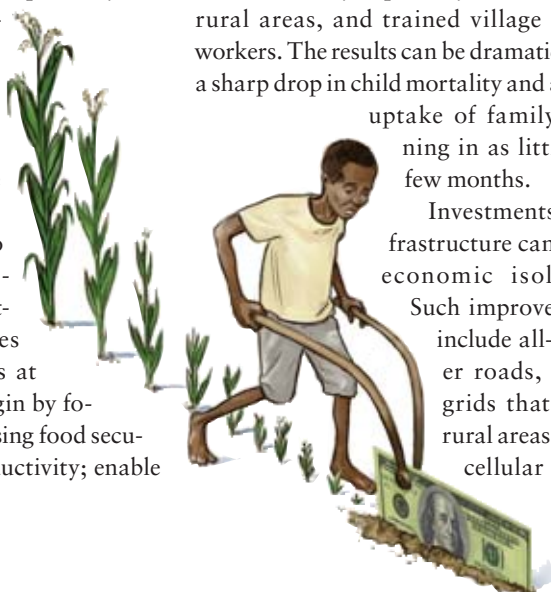
uptake of family planning in as little as a few months.

Investments in infrastructure can break economic isolation. Such improvements include all-weather roads, power grids that reach rural areas, wider cellular phone

coverage, and even broadband Internet services obtained through fiber-optic cables or satellite connections. Linking formerly remote villages to regional and world markets enables them to earn much more cash income through sales of agricultural commodities, processed goods and services.

The Earth Institute at Columbia University, in partnership with the United Nations and the nongovernmental organization Millennium Promise, is putting targeted investments to work in Africa, Asia and Latin America. The early results are enormously positive (learn more at www.millenniumvillages.org). Governments around Africa, including some in former war zones, are now requesting such projects. The World Bank and other donors would be wise to respond favorably, because such investment is the best hope for peace, security and long-term prosperity in impoverished regions. ■

Jeffrey D. Sachs is director of the Earth Institute at Columbia University (www.earth.columbia.edu).



An expanded version of this essay is available at www.SciAm.com/ontheweb

MATT COLLINS

Forum

Full Speed Ahead for an Accelerator

The U.S. must stay competitive in nuclear science

BY C. KONRAD GELBKE



This item probably did not make the front page of your local newspaper, but researchers at the National Superconducting Cyclotron Laboratory (NSCL) at Michigan State University recently produced the heaviest silicon isotope ever observed. After slamming a beam of calcium ions into a tungsten target, scientists analyzed the reaction prod-

ucts and identified three silicon 44 ions, each with 14 protons and 30 neutrons. (Ordinary silicon has 14 neutrons.) Given that the hefty nuclei survived for only a tiny fraction of a second before decaying, the achievement may not sound earthshaking, but this kind of nuclear research is vitally important. Studying the properties of rare isotopes can help astrophysicists explain how the reactions in exploding stars generated the elements that make

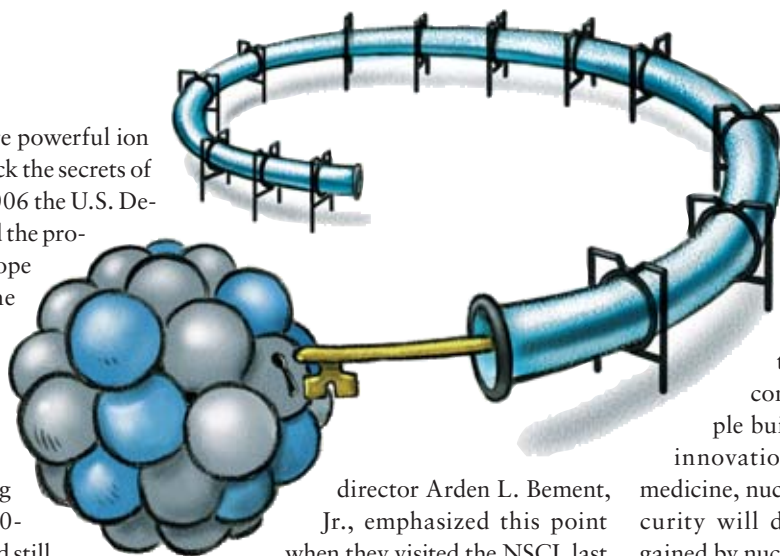
up Earth and all the other planets. Isotopes with the appropriate chemical and radiological characteristics could be incorporated into new cancer treatments. And a better understanding of exotic nuclei could even explain why the universe is rich in matter but almost devoid of antimatter.

For the past several years, scientists at the NSCL (where I have been the director since 1992) and the Argonne National Laboratory in DuPage County, Illinois,

NSCL

have sought to build a more powerful ion accelerator that could unlock the secrets of the nucleus. In February 2006 the U.S. Department of Energy delayed the proposed \$1-billion Rare Isotope Accelerator and asked the physics community to consider planning a cheaper facility. Last December a National Academy of Sciences committee released a 124-page report concluding that a slimmed-down \$550-million ion accelerator could still perform valuable work and should be considered a high priority. Scientists in Japan recently fired up the \$380-million Radioactive Isotope Beam Factory, and researchers in Germany and France plan to complete similar facilities within the next four years. The National Academy's report warned that "failure to pursue such a capability will not only lead to the forfeiture of U.S. leadership but will likely erode our current capability and curtail the training of future American nuclear scientists."

One reason to heed this warning is that a robust program of nuclear research is essential to keeping the U.S. competitive in the 21st century. Senator Carl Levin of Michigan and National Science Foundation



director Arden L. Bement, Jr., emphasized this point when they visited the NSCL last fall. The NSCL has a user community of more than 700 researchers from 100 institutions and 35 countries. With rising globalization and the incumbent need to collaborate across national borders, the U.S. gains a great advantage from making sure that prominent international research and education hubs remain based in this country. Such centers offer the best possible hands-on education to their resident students and young scientists.

Of course, for those of us who work in the field, the science itself—the production and study of nuclear species that do not exist on Earth but are important in the cosmos—provides the most compelling reason to build a new facility. In addition to

revealing clues about the evolution of stars, this work also provides important cross-disciplinary links to broad scientific themes, such as the self-organization of matter and the emergence of complex structures from simple building blocks. Many future innovations in materials research, medicine, nuclear energy and national security will depend on the knowledge gained by nuclear investigators.

In nuclear science, as in so many other endeavors, the prospect for new discoveries attracts the best minds. High-energy physicists who investigate the nature of matter are currently flocking to the Large Hadron Collider near Geneva, which is expected to begin operation next year. But the U.S. still has time to preserve its competitiveness in the equally exciting field of nuclear physics. If we act now, we can lead. If we choose inaction, we must follow. ■

C. Konrad Gelbke is director of the NSCL at Michigan State University. The laboratory's plans for a next-generation isotope science facility are available at www.nscl.msu.edu/lisf

MATT COLLINS

Skeptic

Rational Atheism

An open letter to Messrs. Dawkins, Dennett, Harris and Hitchens

BY MICHAEL SHERMER



Since the turn of the millennium, a new militancy has arisen among religious skeptics in response to three threats to science and freedom: (1) attacks against evolution education and stem cell research; (2) breaks in the barrier separating church and state leading to political preferences for some faiths over others; and (3) fundamentalist terrorism here and abroad. Among many metrics available to track this skeptical movement is the ascension of four books to the august heights of the *New York Times* best-seller list—Sam Harris's

Letter to a Christian Nation (Knopf, 2006), Daniel Dennett's *Breaking the Spell* (Viking, 2006), Christopher Hitchens's *God Is Not Great* (Hachette Book Group, 2007) and Richard Dawkins's *The God Delusion* (Houghton Mifflin, 2006)—that together, in Dawkins's always poignant prose, "raise consciousness to the fact that to be an atheist is a realistic aspiration, and a brave and splendid one. You can be an atheist who is happy, balanced, moral and intellectually fulfilled." Amen, brother.

Whenever religious beliefs conflict with scientific facts or violate principles of political liberty, we must respond with appro-

BRAD SWONETZ

THE EDITORS' BLOG

Posts from SciAm Observations, see www.SciAm.com/blog

Birth Order and IQ: An Environmental Lesson

Posted by Philip Yam, June 22, 2007

The Norwegian study concluding that families' eldest male children have higher IQs than their later-born brothers will surely inspire heated discussion during Festivus and other family gatherings. But focusing on how it might tap into unresolved sibling tension would miss a larger point about IQ scores, intelligence and the environment.

In this latest study, appearing in the June 22 *Science*, two investigators from Oslo studied 241,300 Norwegians, focusing on men. Not only did they find that first-borns had higher IQs (103.2) than second-borns (100.4) and third-borns (99), they also say that social rank, rather than birth order per se, is the determining factor. Basically first-borns have the advantage of more resources—parents can devote more time, money and energy to them. These advantages slip to the next child after the first one dies. In such cases, the second-borns' scores rose, to an average IQ of 102.6. The findings also support the notion that tutoring of their younger siblings helps the older kids master subjects and score higher on tests.

The study illustrates the power of the environment on IQ. The best example is the Flynn effect, which shows that IQ scores have been rising over the generations, a rise attributable to the environment more so than to genes.

Older siblings may have some IQ bragging rights because of this study, but that would be the wrong lesson to take home. As Benedict Carey points out in the *New York Times* story covering this, plenty of great thinkers were later-borns, including Charles Darwin (fifth of six), René Descartes (third of three) and Nicolaus Copernicus (fourth of four). And if you're one of those parents who would play Mozart to your kids while they are fetuses (on the belief that even if the Mozart effect is false, it cannot hurt), here is my suggestion based on this study: have your kids volunteer to tutor less privileged individuals. Even if it does not boost your kids' IQ score, it will definitely do a lot of good.

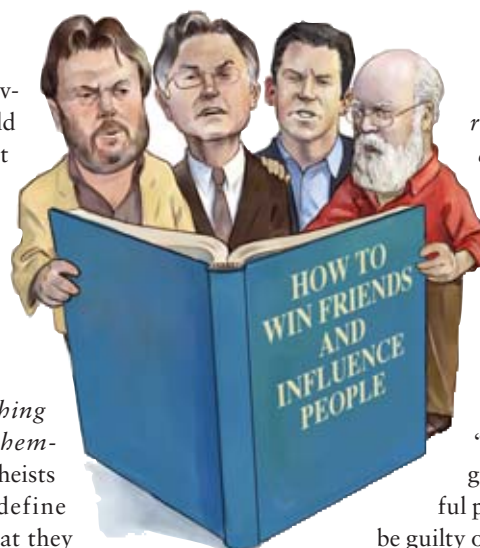
priate aplomb. Nevertheless, we should be cautious about irrational exuberance. I suggest that we raise our consciousness one tier higher for the following reasons.

1. *Anti-something movements by themselves will fail.* Atheists cannot simply define themselves by what they do not believe. As Austri-

an economist Ludwig von Mises warned his anti-Communist colleagues in the 1950s: "An anti-something movement displays a purely negative attitude. It has no chance whatever to succeed. Its passionate diatribes virtually advertise the program they attack. People must fight for something that they want to achieve, not simply reject an evil, however bad it may be."

2. *Positive assertions are necessary.* Champion science and reason, as Charles Darwin suggested: "It appears to me (whether rightly or wrongly) that direct arguments against Christianity & theism produce hardly any effect on the public; & freedom of thought is best promoted by the gradual illumination of men's minds which follow[s] from the advance of science. It has, therefore, been always my object to avoid writing on religion, & I have confined myself to science."

3. *Rational is as rational does.* If it is our goal to raise people's consciousness to the wonders of science and the power of reason, then we must apply science and reason to our own actions. It is irrational to take a hostile or condescending attitude toward religion because by doing so we virtually guarantee that religious people will respond in kind. As Carl Sagan cautioned in "The Burden of Skepticism," a 1987 lecture, "You can get into a habit of thought in which you enjoy making fun of all those other people who don't see things as clearly as you do. We have to guard carefully against it."



4. *The golden rule is symmetrical.* In the words of the greatest consciousness raiser of the 20th century, Martin Luther King, Jr., in his epic "I Have a Dream" speech: "In the process of gaining our rightful place, we must not be guilty of wrongful deeds.

Let us not seek to satisfy our thirst for freedom by drinking from the cup of bitterness and hatred. We must forever conduct our struggle on the high plane of dignity and discipline." If atheists do not want theists to prejudge them in a negative light, then they must not do unto theists the same.

5. *Promote freedom of belief and disbelief.* A higher moral principle that encompasses both science and religion is the freedom to think, believe and act as we choose, so long as our thoughts, beliefs and actions do not infringe on the equal freedom of others. As long as religion does not threaten science and freedom, we should be respectful and tolerant because our freedom to disbelieve is inextricably bound to the freedom of others to believe.

As King, in addition, noted: "The marvelous new militancy which has engulfed the Negro community must not lead us to a distrust of all white people, for many of our white brothers, as evidenced by their presence here today, have come to realize that their destiny is tied up with our destiny. And they have come to realize that their freedom is inextricably bound to our freedom."

Rational atheism values the truths of science and the power of reason, but the principle of freedom stands above both science and religion. ■

Michael Shermer is publisher of *Skeptic* (www.skeptic.com). His latest book is *Why Darwin Matters* (Henry Holt, 2006).

MATT COLLINS

Anti Gravity

What's the Big Idea?

When the lightbulb above your head is truly incendiary

BY STEVE MIRSKY



Recently I entered a bookstore. After ambling by the coffee and dessert area and passing the CDs and DVDs, I found actual books! The title of one of them stopped me: *What Is Your Dangerous Idea?* Potential answers came quickly:

Test the hypothesis first posited as a child that a red towel tied around the neck will indeed confer the ability to fly.

Go all in against a poker player named after a city or state, such as Amarillo or Colorado.

Wear a Yankees jacket in the bleachers at Fenway Park.

Carry a book called *What Is Your Dangerous Idea?* through airport security.

A closer inspection, however, revealed the book to be a collection of dangerous *intellectual* ideas, concepts that in many quarters might be considered to be literally unthinkable. In his introduction, Harvard University psychologist Steven Pinker (who came up with the dangerous idea idea) throws examples around, including: “Do women, on average, have a different profile of aptitudes and emotions than men?” “Is homosexuality the symptom of an infectious disease?” “Is morality just a product of the evolution of our brains, with no inherent reality?” To test whether the mere asking of these questions might be dangerous, pose the first to Hillary Clinton, the second to Ellen DeGeneres and the third to William J. Bennett, author of the *Book of Virtues*, who nonetheless lost millions in venues dominated by guys named Amarillo and Colorado.

The book is edited by John Brockman, editor and publisher of

FLYNN/LARSEN

THINK 18-wheel air freshener

Edge (www.edge.org), a Web site devoted to “inquiry into and discussion of intellectual, philosophical, artistic, and literary issues, as well as to work for the intellectual and social achievement of society,” and whose “informal membership includes some of the most interesting minds in the world.” One can therefore find in Edge critiques of the antievolution essay of presidential candidate Sam Brownback, but not the antievolution essay itself. (The *New York Times* published that work, which immediately dropped P. J. O’Rourke down to second funniest conservative commentator.)

In his preface, Brockman notes that a provocative question is an annual Edge feature. The roots of this exercise date back to 1971, when artist James Lee Byars identified his 100 most brilliant people on the planet. His plan was to have them ask one another the same questions they had been asking themselves. Byars “called each of them,” Brockman explains, “and asked them what questions they were asking themselves. The result: 70 people hung up on him.” Which may prove that Byars was in fact only 70 percent successful in his personal assessment of brilliant minds.

The book includes 108 contributions, some of which go egg-head-to-egghead. For example, physicist and computer scientist



W. Daniel Hillis’s dangerous idea is “the idea that we should all share our most dangerous ideas.” Whereas psychologist Daniel Gilbert’s dangerous idea is “the idea that ideas can be dangerous.” I both agree and disagree with both.

Nature’s chief news and features editor Oliver Morton has the dangerous idea that “our planet is not in peril,” although he quite rightly points out that many *inhabitants* of the planet are in great jeopardy because of environmental crises. Actually, George Carlin covered this territory years ago when he said, “The planet is fine. The *people* are f*^#ed... the planet’ll shake us off like a bad case of fleas.”

My personal favorite entry is that of philosopher and psychologist Nicholas Humphrey, who knows a dangerous idea when he sees one and so simply quotes Bertrand Russell’s truly treacherous notion: “I wish to propose... a doctrine which may, I fear, appear wildly paradoxical and subversive. The doctrine in question is this: that it is undesirable to believe in a proposition when there is no ground whatsoever for supposing it true.” The danger of ignoring this doctrine can almost certainly be found in the politics or world events stories on the front page of today’s *New York Times*. On whatever day you read this. ■

MATT COLLINS

Diesel engines are renowned for their durability and outstanding fuel economy. Oil and natural gas industry engineers now

Ultra low sulfur diesel and advanced engines will mean 90% less emissions

make diesel even better.

They are producing an advanced fuel, ultra low sulfur diesel (ULSD), to help new, efficient diesel engines run

even cleaner. Today this clean, efficient fuel is available across America. When combined with the advanced diesel engines now available for buses, trucks and cars, ULSD will ultimately cut emissions by 90 percent. Now that’s blue-sky thinking.

EnergyFutureusa.org

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What Visions in the Dark of Light

Lene Vestergaard Hau made headlines by slowing light to below highway speed. Now the ringmaster of light can stop it, extinguish it and revive it—and thereby give quantum information a new look **BY MARGUERITE HOLLOWAY**

Lene Vestergaard Hau's favorite time of year is midsummer's eve, when the sky in her native Denmark turns a light metallic blue and the sun stays set for only a few hours. "It never really gets dark," she says one May morning in her sunny office at Harvard University. "You have these long, light nights. It is just a wonderful time of year. That is the thing I really miss here." Hau came to the U.S. for postdoctoral work two decades ago, vaulted into a new realm of physics, ignited another one, and has been here since, making the world think differently about the qualities of light.

The speed of light—299,792,458 meters per second in a vacuum—"is an incomprehensibly high speed," Hau says. "If you could somehow tame that to a human level, it would be completely fascinating." That is exactly what the 47-year-old physicist has done: she has forced light to plod, pile up and squeeze into a tiny cage, stay docile in that cage and even vanish, only to reappear some distance off. Light slows all the time: photons passing through water decelerate to roughly 224,844,344 meters per second, and they stop and are obliterated when they hit opaque surfaces. But before Hau's work, light had never lagged to 17 meters per second and, in the same manner, been snuffed out and then revived intact.

Because photons travel far and fast without degrading, they have become the



focus of research to develop quantum computers and improve optical communication. Hau's work is not directly applicable, because her experiments unfold in Bose-Einstein condensates—clusters of supercold atoms acting as one giant collective. Yet her research gets at the root of the challenge of using light to store and

process information. By stopping the light, "you are storing a quantum bit. Conceptually, it is a new kind of memory unit," says Seth Lloyd, a quantum physicist at the Massachusetts Institute of Technology.

Hau, who won a MacArthur Fellowship in 2001, did not plan to be an experimental physicist. Her training was in the theoretical side, although in the 1980s, at home in Denmark and then at CERN near Geneva, she worked on condensed matter. "In doing that, I discovered that people had started to use new techniques of using lasers to cool atoms down to extremely cold temperatures," she recalls. In 1988 Hau traveled to the U.S. to meet researchers, give talks and satisfy a desire to "see if

LENE VESTERGAARD HAU

HOW TO OUTPACE LIGHT: Uses lasers and Bose-Einstein condensates (atoms at near absolute zero) to slow light to 17 meters per second—bicycle-racing speed—or stop it completely.

WARMING TO THE COLD: Began studying condensates shortly after their creation in 1995 but chose a different path from other researchers: "In the back of your head, you know you are moving into totally new territory, and that is where you open up new possibilities."

"WHAT VISIONS FROM THE DARK OF LIGHT," FROM SAMUEL BECKETT'S COMPANY, 1979; PHOTOGRAPH BY KATHLEEN DOOHER



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this country was really like the movies.” Which, she decided, it was: big, with big cars and talkative, open people.

One of Hau’s visits was to the Rowland Institute in Cambridge, Mass., a small non-profit that joined Harvard five years ago. There she met physicists Michael Burns and Jene A. Golovchenko; both encouraged her to explore cold matter, even though neither worked in that emerging field. “I could have gone to a more established place, but it seemed that that would be too predictable,” Hau says.

Hau set about designing a way to get a constant supply of sodium atoms in a vacuum. She then started cooling her sodium atoms toward absolute zero, and on mid-summer’s eve in 1997 she made “some really big, fat” Bose-Einstein condensates. This form of matter had been hypothesized but never created until three scientists—now Nobel laureates—managed to do so in 1995. Hau intended to use light to probe the properties of this new species when she decided to use the condensate to play with light instead. In 1999, in a now famous finding, Hau shone laser light on a condensate, causing photons to creep along inside it. “It was a very, very tricky experiment because it was just on the borderline of what was possible,” she says [see “Frozen Light,” by Lene Vestergaard Hau; SCIENTIFIC AMERICAN, July 2001].

What happens is this: The condensate contains sodium atoms held in place by a magnetic field and illuminated by a “coupling” laser that serves to make the condensate transparent to a specific frequency of light. When photons of that frequency, emitted in a short pulse by a “probe” laser, hit the condensate, they trigger a quantum dark state. This means the sodium atoms enter superposition—they are in two energy states simultaneously. As the photons encounter these atoms, they become entangled with them. The front edge of the light pulse slows, and the back edge catches up, compressing the light like a concertina into the 100-micron-thick condensate.

Light had been slowed experimentally



Hau's optics equipment slowed light to 17 meters per second—then stopped and started it.

before by a factor of 165 (to 1,816,923 meters per second or so) using the transparency technique Hau employs. But “by observing light going 17 meters per second, it gave impetus to a worldwide effort in that direction,” says Stephen E. Harris of Stanford University, who collaborated with Hau and first demonstrated electromagnetically induced transparency and slowed light with it in the early 1990s. Researchers have now slowed light in hot gases as well as in crystals and semiconductors at room temperature.

Slowing light led Hau to stopping and starting it. In 2001 she and her colleagues turned off the coupling laser and discovered that the light pulse in the condensate disappeared; its characteristic shape, amplitude and phase, however, were imprinted on the sodium atoms. When the coupling laser came back on, the incoming jolt of energy caused the altered sodium atoms to shift energy levels, in the process releasing a light pulse of the exact phase and amplitude as the one originally sent in by the probe laser. Light had come in with information, conveyed that information to matter and disappeared. Then matter had produced light with that same information. “That is how we preserve information in the system. It is not some random thing that you have no control over,” Hau says.

This year Hau and two members of her lab, Naomi S. Ginsberg and Sean R. Garner, took matters a step further by transmitting the light pulse's characteristics between two condensates. They sent a pulse from the probe laser into the first condensate, where, as expected, it slowed. Next they turned off the coupling laser. The light pulse from the probe disappeared, but not before it had communicat-

ed information about its amplitude and phase to the sodium atoms. These atoms also had momentum from the photonic collision, momentum that propelled them out of the first condensate, across a tiny gap and into the second condensate. Once the atoms—a matter copy of the extinguished light pulse—arrived, the coupling laser was turned back on; the atoms, eager to join the second condensate, shifted energy levels, releasing photons with the exact phase and amplitude of those that had entered the first condensate.

As Hau and Lloyd note, transferring light into matter and back again means that quantum information could be processed. “Basically, the probe light would carry quantum information over long distances in optical fibers,” Hau explains. “Then if you want to do something to it, you read it into matter. We can use matter dynamics to change optical information.” Light interactions in Bose-Einstein condensates have also produced unexpected phenomena—for example, tornadolike storms in the condensates sometimes act like billiard balls, bouncing off one another, and sometimes annihilate one another. “It is a total zoo,” Hau says excitedly. “The experiments show much more detail than the calculations did.”

Hau's many experiments kept her from the special blue of midsummer's eve again this year. But she brought Scandinavia to her new suite of labs: the walls are yellow and orange, and there is plenty of light wood. “Colors are very important,” she says. “Colors and light, they are the way you feel how happy you are.” Hau and poet Robert Frost seem of the same mind: “The light was what it was all about / I would not go in till the light went out / It would not go out till I came in.” ■

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A QUESTION OF SUSTENANCE

Globalization ushered in a world in which more than a billion are overfed. Yet hundreds of millions still suffer from hunger's persistent scourge

KEY CONCEPTS

- The world escaped the dire scenarios of mass starvation predicted during the 1960s.
- A nutrition transition has occurred in which developing countries harbor both hunger and obesity concurrently.
- Overall, obesity is more of a public health problem than hunger, yet few good solutions exist to deal with the emerging epidemic.
- Farmers produce enough for everyone. But hunger persists because of political conflict, natural disasters and rural poverty.
- Agronomists continue to explore whether genetically modified crops can help feed the world, while industrial nations wrestle with nutritionism, the notion of food as medicine.

—The Editors

By Gary Stix

In 1963 some 200,000 Indians in West Bengal and Assam faced imminent starvation. A few years later drought caused severe food shortages in the nearby state of Bihar. Against a backdrop of such reports, biologist Paul Ehrlich speculated in his 1968 book *The Population Bomb* that, within just a few years, hundreds of millions would starve to death, as inexorable population growth outstripped limited resources.

This neo-Malthusian scenario never came to pass. For India, the green revolution in agriculture averted a “ship to mouth” existence in which foreign food aid would be needed indefinitely to stave off Ehrlich’s worst-case prognostications. In the ensuing 40 years, India has undergone a radical makeover and now graces magazine covers as an emerging economic giant. The turn-of-the-century developing world now often confronts more of a problem with fat than it does with famine—a sociological spin-off of globalization known as the nutrition transition. The millennium marked the first time

that the overweight equaled the number of the undernourished worldwide, and, as a demographic, the overnourished 1.3 billion now surpass the hungry by several hundred million.

Rich and poor now fret about many of the same things at the dinner table. Coca-Colonization—a term that even crops up in academic papers—has built a global infrastructure for *comida chatarra*, the Mexican label for junk food. Coca-Cola distributors ink exclusive agreements down to the level of neighborhood *tiendas*, supplying shopkeepers with refrigerators and point-of-sale materials. Mexicans now take in more calories from sugared drinks than Americans do. In tandem, the rise of the U.S.-style supermarket has promoted widespread adoption of corn, soy and other vegetable oils.

The green revolution forestalled mass starvation, but comparable technological ingenuity has largely failed to stem global expansion in waist sizes. An understanding of the endocrinology, neurology and genetics of obesity has slowly emerged. Scientists have even discovered



a gene for fidgeting that promotes the burning of calories. But these insights have yet to produce a good diet pill. The weight-loss drug combination known as Fen-Phen was yanked from the market in 1997 after reports of heart problems. And orlistat (alli) is now sold without a prescription—a consequence, according to some doctors, of its mixed record of effectiveness as a prescription medicine. If it really worked well, physician prescriptions would have brought in blockbuster billions in yearly revenues to GlaxoSmithKline.

Drugmakers have not given up. They are investigating molecules that block brain and gut chemicals that stimulate appetite, along with others that increase the rate of energy expenditure. But a drug will not address the psychological foibles that threaten to undermine the best of treatments. Recent behavioral research

shows that gulping diet pills encourages consumers to yield to temptations for double bacon cheeseburgers and weekends of sitting on the couch watching *Sopranos* reruns. Side effects, too, are a constant preoccupation when tweaking pathways that regulate something as primal as eating. In June, Sanofi Aventis withdrew an application for a proposed weight-loss drug, rimonabant (Acomplia), that may provoke suicidal thoughts. An FDA advisory panel had recommended against its approval.

Following a regimen of eating less and exercising more seems like the simplest bet. Yet even a puritanical way of life comes loaded with controversy. A 2005 study revealed that the moderately overweight have a lower overall death rate than those with bathroom-scale readings in the healthy range. Ever since, the academic nutrition community, steeped in the rhetoric of obesity epidemics, has lobbed broadsides at those blasphemous results.

If most diets do not work in the long run—as much evidence does suggest—what are the overweight to do without a pill or a plan? The fit-but-fat movement advocates staying active combined with diminished worries about one's body mass index. Embracing cultural norms, rather than epidemiology, a few take this argument further. Rural women from Niger shun thinness, and some urban, male hip-hoppers (Heavy D and the Boo-Yaa T.R.I.B.E. among them) embrace excess adiposity, giving new meaning to the word “phat.”

The nutrition transition is by no means monolithic. A visitor to a modest home in Indonesia might find a corpulent child sitting on a living room couch alongside an undernourished sibling, a testament to the paradoxical effects of diets loaded with sugar and vegetable oils. The world produces enough food to feed everyone from West Palm Beach to Pyongyang. But getting rice from paddy to bowl often still poses challenges. Although the number of the world's hungry has fallen, undernourishment persists: hundreds of millions do not receive enough calories every day.

The green revolution, meanwhile, may be pushing its own limits of growth. Whereas cereal production has climbed steadily since the 1960s, when farmers in the developing world first started planting hybrid grains and deploying fertilizers, irrigation and pesticides, the amount of land available for farming remains the same. Heavy pesticide usage may also limit further gains because of pollution of drinking water.

EXCESS HEFT—and its ensuing health complications—affects adults and children in countries rich and poor. Still, 800 million or so do not have enough to eat.



CONSTANTINE MANOS/Magnum (top); SCHWARZBACH/Peter Arnold, Inc. (bottom)

Will Gene Follow Green?

In theory, a “gene revolution” based on genetically modified crops could make up for the inadequacies of the green revolution. The adoption of new practices in the 1960s, fueled by subsidies from governments and transnational groups, took place almost overnight and boosted yields immediately, but biotech crops for the developing world have yet to prove themselves. The private sector purveys genetically modified organisms (GMOs), sometimes charging pro-

hibitive rates that put seed stocks beyond the budgets of small- and medium-size Third World farms. Although a few developing countries have tried GMO corn or soybeans with some success, the promise of the technology as an aid to a specific region’s development—gene-altered crops that can survive drought or grow in saline soil—has yet to be realized on a commercial scale.

Fat and famine coexist in developing countries, but the industrial world wrestles with its own peculiar dietary confusion. Carefully constructed dietary food plans prescribe an exact number of daily servings for meat, dairy, fruits and vegetables. Despite its revision in recent years, the U.S. Department of Agriculture’s food pyramid still receives a heaping portion of disdain from many nutritionists.

The scientific basis for precision national meal planning is decidedly scant. Most food research relies on tracking a single nutrient and fails to identify other contributors, whether genetic or behavioral, that can lead to such killers as coronary artery disease or diabetes. The necessity of oversimplification helps to explain the constant overturning of the prevailing wisdom with studies claiming that eating more fiber does not prevent cancer and that low-fat diets do nothing to prevent heart disease and colorectal cancer. Marion Nestle, author of “Eating Made Simple,” the lead article in this single-topic issue, beginning on page 60, tries to sort things out for the perplexed supermarket patron by coining a mantra: eat less, move more, consume plenty of fruits, vegetables and whole grains, and eschew junk food.

Entreaties to keep it simple do not stray far from what might be called the “Mark Twain diet.” Twain reduced the complexities of dietary energy balances to a single sentence: “Part of the secret of success in life is to eat what you like and let the food fight it out inside.” Other neo-Twainians—Michael Pollan, author of the much heralded *The Omnivore’s Dilemma* (Penguin, 2006), among them—argue for the pleasures of food, while forgoing nutritionism, the quest for nutrients as medicine, a pursuit that may, paradoxically, fail to enhance health. Pollan urges the consumer to “pay more, eat less” by buying organics or other quality foodstuffs that conserve taste along with nutritional value. If one follows his reasoning, the culinary arts and nutritional sciences need not remain at loggerheads. Both should roundly reject the vitamin-fortified meal-replacement bar.

GLOBAL REACH of the obesity epidemic extends to developing countries, spurred in part by the presence of junk food.



XIE HUANCHI/Xinhua/AP Photo (top); THE ENG KOON AP Photo (bottom)

EATING MADE SIMPLE

How do you cope with a mountain of conflicting diet advice?

By Marion Nestle

KEY CONCEPTS

- Nutrition advice is confusing. Scientists have difficulty deriving clear guidelines because a study of an individual nutrient fails to produce an understanding of what happens to it when mixed with other nutrients in the body.
- The picture becomes more clouded because industry groups constantly press their message to both government agencies and consumers about the benefits of eating particular food products.
- The simplest message may be the best: do not overeat, exercise more, consume mostly fruits, vegetables and whole grains, and avoid junk foods.

—The Editors

As a nutrition professor, I am constantly asked why nutrition advice seems to change so much and why experts so often disagree. Whose information, people ask, can we trust? I'm tempted to say, "Mine, of course," but I understand the problem. Yes, nutrition advice seems endlessly mired in scientific argument, the self-interest of food companies and compromises by government regulators. Nevertheless, basic dietary principles are not in dispute: eat less; move more; eat fruits, vegetables and whole grains; and avoid too much junk food.

"Eat less" means consume fewer calories, which translates into eating smaller portions and steering clear of frequent between-meal snacks. "Move more" refers to the need to balance calorie intake with physical activity. Eating fruits, vegetables and whole grains provides nutrients unavailable from other foods. Avoiding junk food means to shun "foods of minimal nutritional value"—highly processed sweets and snacks laden with salt, sugars and artificial additives. Soft drinks are the prototypical junk food; they contain sweeteners but few or no nutrients.

If you follow these precepts, other aspects of the diet matter much less. Ironically, this advice has not changed in years. The noted cardiologist Ancel Keys (who died in 2004 at the age of

JAMES PORTO



OVERABUNDANCE of food
choices confronts
shoppers and diners
every day.





ORGANIC FOODS have been shown to leave people who eat them with fewer synthetic pesticides in their bodies than are found in those who consume conventional foods. Proving that organics contain more vitamins or antioxidants is more difficult, but preliminary studies clearly suggest that they do.

overall dietary pattern that really counts most.

For chronic diseases, single nutrients usually alter risk by amounts too small to measure except through large, costly population studies. As seen recently in the Women's Health Initiative, a clinical trial that examined the effects of low-fat diets on heart disease and cancer, participants were unable to stick with the restrictive dietary protocols. Because humans cannot be caged and fed measured formulas, the diets of experimental and control study groups tend to converge, making differences indistinguishable over the long run—even with fancy statistics.

It's the Calories

Food companies prefer studies of single nutrients because they can use the results to sell products. Add vitamins to candies, and you can market them as health foods. Health claims on the labels of junk foods distract consumers from their caloric content. This practice matters because when it comes to obesity—which dominates nutrition problems even in some of the poorest countries of the world—it is the calories that count. Obesity arises when people consume significantly more calories than they expend in physical activity.

America's obesity rates began to rise sharply in the early 1980s. Sociologists often attribute the “calories in” side of this trend to the demands of an overworked population for convenience foods—prepared, packaged products and restaurant meals that usually contain more calories than home-cooked meals.

But other social forces also promoted the calorie imbalance. The arrival of the Reagan administration in 1980 increased the pace of industry deregulation, removing controls on agricultural production and encouraging farmers to grow more food. Calories available per capita in the national food supply (that produced by American farmers, plus imports, less exports) rose from 3,200 a day in 1980 to 3,900 a day two decades later [see box on opposite page].

The early 1980s also marked the advent of the “shareholder value movement” on Wall Street. Stockholder demands for higher short-term returns on investments forced food com-

100) and his wife, Margaret, suggested similar principles for preventing coronary heart disease nearly 50 years ago [see sidebar at left].

But I can see why dietary advice seems like a moving target. Nutrition research is so difficult to conduct that it seldom produces unambiguous results. Ambiguity requires interpretation. And interpretation is influenced by the individual's point of view, which can become thoroughly entangled with the science.

Nutrition Science Challenges

This scientific uncertainty is not overly surprising given that humans eat so many different foods. For any individual, the health effects of diets are modulated by genetics but also by education and income levels, job satisfaction, physical fitness, and the use of cigarettes or alcohol. To simplify this situation, researchers typically examine the effects of single dietary components one by one.

Studies focusing on one nutrient in isolation have worked splendidly to explain symptoms caused by deficiencies of vitamins or minerals. But this approach is less useful for chronic conditions such as coronary heart disease and diabetes that are caused by the interaction of dietary, genetic, behavioral and social factors. If nutrition science seems puzzling, it is because researchers typically examine single nutrients detached from food itself, foods separate from diets, and risk factors apart from other behaviors. This kind of research is “reductive” in that it attributes health effects to the consumption of one nutrient or food when it is the

OLD ADVICE STILL HOLDS TRUE

In 1959 Ancel and Margaret Keys offered the following—familiar and still useful—precepts regarding nutrition and activity:

- Do not get fat; if you are fat, reduce.
- Restrict saturated fats: fats in beef, pork, lamb, sausages, margarine and solid shortenings; fats in dairy products.
- Prefer vegetable oils to solid fats but keep total fats under 30 percent of your diet calories.
- Favor fresh vegetables, fruits and nonfat milk products.
- Avoid heavy use of salt and refined sugar.
- Good diets do not depend on drugs and fancy preparations.
- Get plenty of exercise and outdoor recreation.

panies to expand sales in a marketplace that already contained excessive calories. Food companies responded by seeking new sales and marketing opportunities. They encouraged formerly shunned practices that eventually changed social norms, such as frequent between-meal snacking, eating in book and clothing stores, and serving larger portions. The industry continued to sponsor organizations and journals that focus on nutrition-related subjects and intensified its efforts to lobby government for favorable dietary advice. Then and now food lobbies have promoted positive interpretations of scientific studies, sponsored research that can be used as a basis for health claims, and attacked critics, myself among them, as proponents of “junk science.” If anything, such activities only add to public confusion.

FOOD FACTOIDS

To reduce your weight by a pound of fat a week, eat 500 fewer calories each day.

Carbohydrates and proteins have about 4 calories per gram. Food fats contain more than twice as much: 9 calories per gram. A teaspoon holds about 5 grams.

Alcohol is metabolized in a way that promotes accumulation of fat in the liver, leading to the proverbial beer belly.

An adult expends about 100 calories for every mile walked or run. It takes nearly three miles to burn off the calories in a 20-ounce soft drink.

Supermarkets as “Ground Zero”

No matter whom I speak to, I hear pleas for help in dealing with supermarkets, considered by shoppers as “ground zero” for distinguishing health claims from scientific advice. So I spent a year visiting supermarkets to help people think more clearly about food choices. The result was my book *What to Eat*.

Supermarkets provide a vital public service but are not social services agencies. Their job is to sell as much food as possible. Every aspect of store design—from shelf position to background music—is based on marketing research [see center item on page 68]. Because this research shows that the more products customers see, the more they buy, a store’s objective is to expose shoppers to the maximum number of products they will tolerate viewing.

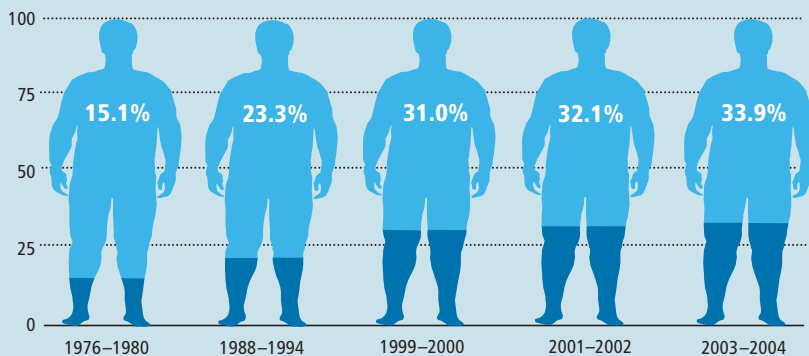
[OBESITY GAINS]

AS FOOD CALORIES SWELL, SO DO WAISTLINES

A substantial rise in U.S. obesity rates during the past few decades was paralleled by increases in the availability of larger portion sizes, total calories, caloric sweeteners and sugary soft drinks in the food supply. The apparent dip in three of these measures (calories, sugars and sugary soft drinks) after 1998 may be explained by greater use of artificial sweeteners and the partial replacement of sugary soft drinks with beverages that are not sweetened with sugars.

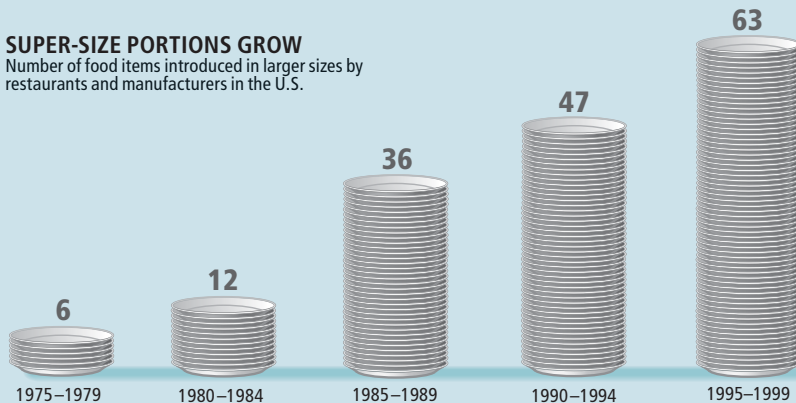
U.S. OBESITY RATES ON THE RISE

Percent of total population (ages 20–74) classified as obese



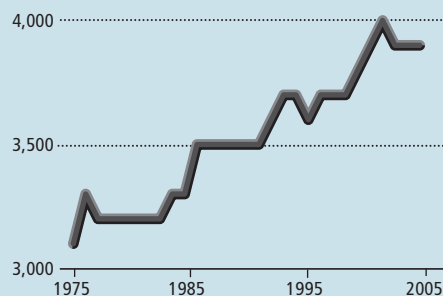
SUPER-SIZE PORTIONS GROW

Number of food items introduced in larger sizes by restaurants and manufacturers in the U.S.



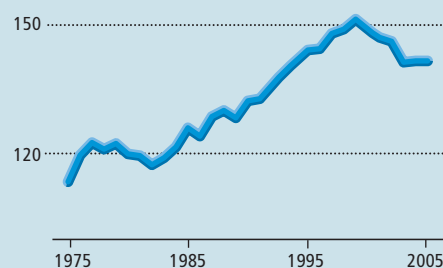
CALORIES AVAILABLE

Per person per day in the U.S. food supply



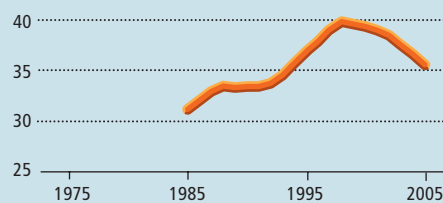
CALORIC SWEETENERS AVAILABLE

Pounds per person in the U.S. food supply



SUGARY SOFT DRINKS AVAILABLE

Gallons per person in the U.S. food supply



If consumers are confused about which foods to buy, it is surely because the choices require knowledge of issues that are not easily resolved by science and are strongly swayed by social and economic considerations. Such decisions play out every day in every store aisle.

Are Organics Healthier?

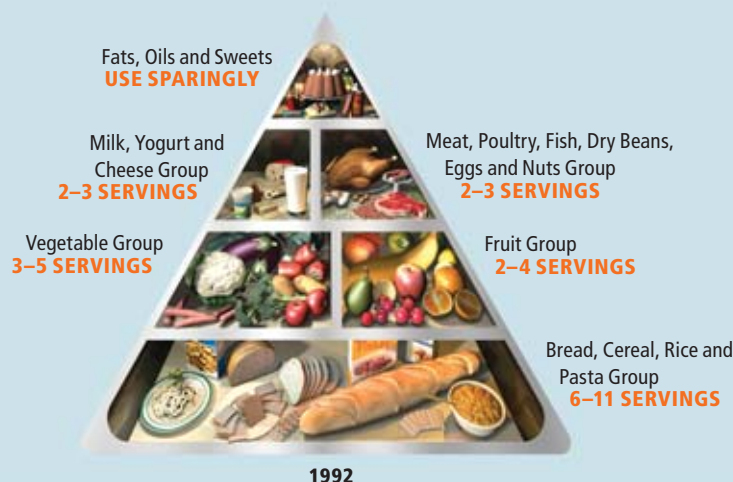
Organic foods are the fastest-growing segment of the industry, in part because people are willing to pay more for foods that they believe are healthier and more nutritious. The U.S. Department of Agriculture forbids producers of “Certified Organic” fruits and vegetables from using synthetic pesticides, herbicides, fertilizers, genetically modified seeds, irradiation or fertil-

izer derived from sewage sludge. It licenses inspectors to ensure that producers follow those rules. Although the USDA is responsible for organics, its principal mandate is to promote conventional agriculture, which explains why the department asserts that it “makes no claims that organically produced food is safer or more nutritious than conventionally produced food. Organic food differs from conventionally grown food in the way it is grown, handled and processed.”

This statement implies that such differences are unimportant. Critics of organic foods would agree; they question the reliability of organic certification and the productivity, safety and health benefits of organic production methods.

[GOVERNMENT ADVICE]

FLAWED FOOD PYRAMIDS



Whether you found the food pyramid created by the U.S. Department of Agriculture in 1992 beneficial or not, it was at least simple to use. The familiar triangular nutrition guide suggested how much of each food category—grains, dairy products, fruits and vegetables, meats and fats, oils and sweets—one should eat every day.

But in my opinion, the USDA’s 2005 replacement, MyPyramid, is a disaster. The process the agriculture agency employed to replace the 1992 food pyramid (*left*) has been kept secret. It remains a mystery, for example, just how the department came up with a design for a new food guide that emphasizes physical activity but is devoid of food (*right*). According to the USDA staff, people should keep physically active, eat in moderation, make personalized food choices, eat a variety of foods in the recommended number of servings, and pursue gradual dietary improvement. The color and width of the vertical bands of MyPyramid are meant to denote food groups and servings, but the only way to know this in detail is to log on to a computer. Users must go to www.pyramid.gov and type in gender, age and activity level to obtain a “personalized” dietary plan at one of a dozen calorie levels.

People who seek advice from this site, and millions have, find diet

plans notable for the large amounts of food they seem to recommend and for the virtual absence of appeals to “eat less” or to “avoid” certain foods. Critics, not surprisingly, discern the strong influence of food industry lobbyists here. I myself, for example, am expected to consume four cups of fruits and vegetables, six ounces of grains, five ounces of meat and, of course, three cups of milk a day, along with a couple of hundred “discretionary calories” that I can spend on junk foods. For all its flaws, the 1992 pyramid was easier to understand and use.

What MyPyramid really lacks is any notion of a hierarchical ranking of the items in a single food group in terms of nutritional desirability. The preliminary design of MyPyramid in 2004 looked much like the final version with one critical exception: it illustrated a hierarchy of desirable food choices. The grain band, for instance, placed whole-grain bread at the bottom (a positive ranking), pasta about halfway up (a middle rank) and cinnamon buns at the top (“eat less”). In the final version, the USDA eliminated all traces of hierarchy, presumably because food companies do not want federal agencies to advise eating less of their products, useful as such recommendations might be to an overweight public.

—M.N.

NICK ROTUNDO

SOME OBESE CHILDREN in the U.S. consume 1,000 calories a day (equal to about 59 sugar cubes) in sweetened beverages alone. That is equivalent to more than three 20-ounce bottles of soft drinks.

Meanwhile the organic food industry longs for research to address such criticisms, but studies are expensive and difficult to conduct. Nevertheless, existing research in this area has established that organic farms are nearly as productive as conventional farms, use less energy and leave soils in better condition. People who eat foods grown without synthetic pesticides ought to have fewer such chemicals in their bodies, and they do. Because the organic rules require pretreatment of manure and other steps to reduce the amount of pathogens in soil treatments, organic foods should be just as safe—or safer—than conventional foods.

Similarly, organic foods ought to be at least as nutritious as conventional foods. And proving organics to be more nutritious could help justify their higher prices. For minerals, this task is not difficult. The mineral content of plants depends on the amounts present in the soil in which they are grown. Organic foods are cultivated in richer soils, so their mineral content is higher.

But differences are harder to demonstrate for vitamins or antioxidants (plant substances that reduce tissue damage induced by free radicals); higher levels of these nutrients relate more to a food plant's genetic strain or protection from unfavorable conditions after harvesting than to production methods. Still, preliminary studies show benefits: organic peaches and pears contain greater quantities of vitamins C and E, and organic berries and corn contain more antioxidants.

Further research will likely confirm that organic foods contain higher nutrient levels, but it is unclear whether these nutrients would make a measurable improvement in health. All fruits and vegetables contain useful nutrients, albeit in different combinations and concentrations. Eating a variety of food plants is surely more important to health than small differences in the nutrient content of any one food. Organics may be somewhat healthier to eat, but they are far less likely to damage the environment, and that is reason enough to choose them at the supermarket.

Dairy and Calcium

Scientists cannot easily resolve questions about the health effects of dairy foods. Milk has many



components, and the health of people who consume milk or dairy foods is influenced by everything else they eat and do. But this area of research is especially controversial because it affects an industry that vigorously promotes dairy products as beneficial and opposes suggestions to the contrary.

Dairy foods contribute about 70 percent of the calcium in American diets. This necessary mineral is a principal constituent of bones, which constantly lose and regain calcium during normal metabolism. Diets must contain enough calcium to replace losses, or else bones become prone to fracture. Experts advise consumption of at least one gram of calcium a day to replace everyday losses. Only dairy foods provide this much calcium without supplementation.

But bones are not just made of calcium; they require the full complement of essential nutrients to maintain strength. Bones are stronger in people who are physically active and who do not smoke cigarettes or drink much alcohol. Studies examining the effects of single nutrients in dairy foods show that some nutritional factors—magnesium, potassium, vitamin D and lactose, for example—promote calcium re-

[THE AUTHOR]



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tention in bones. Others, such as protein, phosphorus and sodium, foster calcium excretion. So bone strength depends more on overall patterns of diet and behavior than simply on calcium intake.

Populations that do not typically consume dairy products appear to exhibit lower rates of bone fracture despite consuming far less calcium than recommended [see sidebar on opposite page]. Why this is so is unclear. Perhaps their diets contain less protein from meat and dairy foods, less sodium from processed foods and less phosphorus from soft drinks, so they retain calcium more effectively. The fact that calcium balance depends on multiple factors could explain why rates of osteoporosis (bone density loss) are highest in countries where people eat

the most dairy foods. Further research may clarify such counterintuitive observations.

In the meantime, dairy foods are fine to eat if you like them, but they are not a nutritional requirement. Think of cows: they do not drink milk after weaning, but their bones support bodies weighing 800 pounds or more. Cows feed on grass, and grass contains calcium in small amounts—but those amounts add up. If you eat plenty of fruits, vegetables and whole grains, you can have healthy bones without having to consume dairy foods.

A Meaty Debate

Critics point to meat as the culprit responsible for elevating blood cholesterol, along with raising risks for heart disease, cancer and other

DROPPING WEIGHT... AND KEEPING IT OFF

By Paul Raeburn

This past March, Stanford University researchers published the results of one of the longest and most persuasive comparisons of weight-loss programs ever conducted. Three of the four diets in the study are heavily promoted regimens that have made their originators famous: the Atkins diet and the Zone diet, which both emphasize high-protein foods, and the Ornish diet, a plan that prohibits most fatty foods. The fourth was the no-frills, low-fat diet that most nutrition experts recommend.

The results, published in the *Journal of the American Medical Association*, were a surprise because they seemed to overturn the conventional wisdom. The experts' low-fat diet was beaten by Atkins's steak dinners and bacon-and-egg breakfasts. A year after starting their diets, people on the Atkins plan—which unapologetically endorses high-fat protein such as meats and dairy products to keep dieters sated—had dropped an average of 10 pounds. Subjects on the other diets had lost between three and six pounds (graph on opposite page). And members of the Atkins test group showed no jump in blood cholesterol levels, despite the high levels of cholesterol in their diet.

Reporters jumped on the obvious headlines: "Atkins Fares Best ..." stated the *Washington Post*. "Atkins Beats Zone, Ornish and U.S. Diet Advice," the Associated Press declared. It was the same everywhere else: Atkins had bested the competition.

The newspaper accounts were not wrong. But the lead author of the Stanford study suggests a

different interpretation of the findings. "What happened in our study was very modest weight loss in all four groups," says Christopher D. Gardner, a nutrition scientist at the Stanford Prevention Research Center. All groups also showed improvement in individuals' levels of cholesterol, blood pressure and insulin, even though none of them followed their diet plans exactly. And far from overturning established ideas about low-fat diets, the Stanford investigation provided resounding confirmation of another generally held belief: most people who try to lose weight, on any kind of diet, will succeed, even if many of them regain the weight later.

Contrast those conclusions with the results of another study published in the April issue of *American Psychologist* by researchers at the University of California, Los Angeles. They analyzed 31 long-term diet studies and found, as Gardner said, that most participants did see results—losing about 5 to 10 percent of their total body mass. And they did it while on all kinds of diets. But most also regained all that weight over the longer term, and some put on even more than they had lost. Only a small minority of subjects in the 31 studies kept the extra pounds off. The researchers' conclusion? Eat in moderation and exercise regularly. (This statement parallels similar advice nutritionist Marion Nestle presents in the accompanying article.)

Gardner thinks the traditional exhortation to cut dietary fat has turned out to be a bad message. The public health experts got it wrong, he says: "It totally backfired on us." People who consumed less fat often turned to soda and similar corn-syrup-sweetened products, along with other refined, low-fiber, carbohydrate-rich foods. As a result, "the obesity epidemic has continued to grow. Calories have continued to creep up, and it's been predominantly in the refined carbohydrates."



YO-YO DIETING is unhealthy.

conditions. Supporters cite the lack of compelling science to justify such allegations; they emphasize the nutritional benefits of meat protein, vitamins and minerals. Indeed, studies in developing countries demonstrate health improvements when growing children are fed even small amounts of meat.

But because bacteria in a cow's rumen attach hydrogen atoms to unsaturated fatty acids, beef fat is highly saturated—the kind of fat that increases the risk of coronary heart disease. All fats and oils contain some saturated fatty acids, but animal fats, especially those from beef, have more saturated fatty acids than vegetable fats. Nutritionists recommend eating no more than a heaping tablespoon (20 grams) of saturated fatty acids a day. Beef eaters easily meet or ex-

ceed this limit. The smallest McDonald's cheeseburger contains 6 grams of saturated fatty acids, but a Hardee's Monster Thickburger has 45 grams.

Why meat might boost cancer risks, however, is a matter of speculation. Scientists began to link meat to cancer in the 1970s, but even after decades of subsequent research they remain unsure if the relevant factor might be fat, saturated fat, protein, carcinogens or something else related to meat. By the late 1990s experts could conclude only that eating beef probably increases the risk of colon and rectal cancers and possibly enhances the odds of acquiring breast, prostate and perhaps other cancers. Faced with this uncertainty, the American Cancer Society suggests selecting leaner cuts, smaller portions

The Atkins plan, which advises dieters to be less concerned about fat, steers people toward vegetables and protein and away from sugars and refined carbohydrates. "Maybe low carb is a better simple message to the public than low fat," Gardner says. "We tell them low carb, and they get it. They cut out a couple of sodas or a couple of cookies, and that adds up."

James Hill, a psychologist and authority on weight loss, agrees that the Atkins approach has virtues. "The Atkins diet is a great way to lose weight," he says. But it "is not a way to keep weight off," he asserts. "There's no way you can do it forever."

Hill is not terribly interested in comparing diets or devising new ones. "I think the weight-loss part is something we do pretty well," he says. One of his areas of research con-

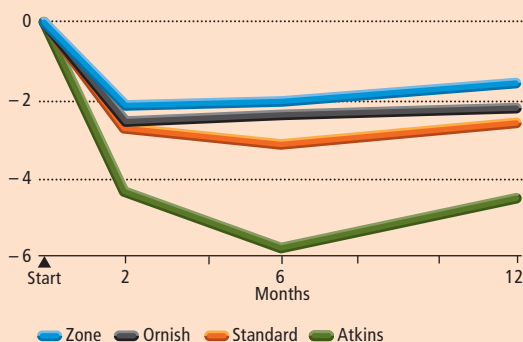
cerns individuals who have reduced their weight and sustained it. Hill and Rena Wing of Brown University have established what they call the National Weight Control Registry to collect data on people who have cut at least 30 pounds and kept them off for a year. Many have lost much more—the average is a 70-pound weight loss maintained for six years. "If you look at how they lost weight, there's no commonality at all," Hill says. But "if you look at how they kept it off, there's a lot of commonality."

The key, he continues, is exercise. "Activity becomes the driver; food restriction doesn't do it. The idea that for the rest of your life you're going to be hungry all the time—that's just silly." People in the registry get an average of an hour of physical activity every day, with some exercising for as much as 90 minutes a day. They also keep the fat in their diet relatively low, at about 25 percent of their calorie intake. Nearly all of them eat breakfast every day, and they weigh themselves regularly. "They tell us two things," Hill says. "The quality of life is higher—life is better than it was before." And "they get to the point with physical activity where they don't say they love it, but they say 'it's part of my life.'"

Hill admits that fitting an hour or more of exercise into the day is difficult, which is why he also focuses on prevention. Many of these people might never have become obese initially if they had exercised a mere 15 to 20 minutes a day. "I think you pay a price for having been obese," he states, "and you have to do a lot of activity to make up for that."

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BATTLE OF THE DIET PLANS
Mean weight change over time (in kilograms)



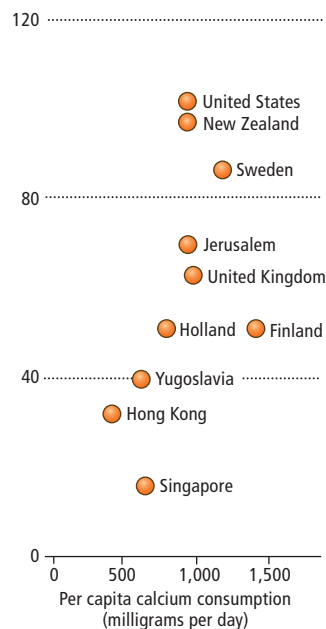
CONTRARY TO EXPECTATIONS, the high-fat Atkins diet produced greater losses than three other popular weight-reduction plans.

NOT MILK?

Surprisingly, some populations that eat few calcium-rich milk products appear in some descriptive studies to have lower rates of hip fractures than others that consume large quantities of dairy foods, despite the fact that diets of the former group contain far less calcium than experts recommend. This observation has not been fully explained.

Calcium intake and hip fractures

Incidence of hip fractures per 100,000 people





and alternatives such as chicken, fish or beans—steps consistent with today’s basic advice about what to eat.

Fish and Heart Disease

Fatty fish are the most important sources of long-chain omega-3 fatty acids. In the early 1970s Danish investigators observed surprisingly low frequencies of heart disease among indigenous populations in Greenland that typically ate fatty fish, seals and whales. The researchers attributed the protective effect to the foods’ content of omega-3 fatty acids. Some subsequent studies—but by no means all—confirm this idea.

Because large, fatty fish are likely to have accumulated methylmercury and other toxins through predation, however, eating them raises questions about the balance between benefits and risks. Understandably, the fish industry is eager to prove that the health benefits of omega-3s outweigh any risks from eating fish.

Even independent studies on omega-3 fats can be interpreted differently. In 2004 the National Oceanic and Atmospheric Administration—for fish, the agency equivalent to the USDA—asked the Institute of Medicine (IOM) to review studies of the benefits and risks of consuming seafood. The ensuing review of the research on heart disease risk illustrates the challenge such work poses for interpretation.

The IOM’s October 2006 report concluded that eating seafood reduces the risk of heart disease but judged the studies too inconsistent to decide if omega-3 fats were responsible. In contrast, investigators from the Harvard School of Public Health published a much more positive report in the *Journal of the American Medical*

OMEGA-3 FATTY ACIDS, which are thought by some researchers to protect against heart disease, are found in oily fish such as salmon and trout.

Association that same month. Even modest consumption of fish omega-3s, they stated, would cut coronary deaths by 36 percent and total mortality by 17 percent, meaning that not eating fish would constitute a health risk.

Differences in interpretation explain how distinguished scientists could arrive at such different conclusions after considering the same studies. The two groups, for example, had conflicting views of earlier work published in March 2006 in the *British Medical Journal*. That study found no overall effect of omega-3s on heart disease risk or mortality, although a subset of the original studies displayed a 14 percent reduction in total mortality that did not reach statistical significance. The IOM team interpreted the “nonsignificant” result as evidence for the need for caution, whereas the Harvard group saw the data as consistent with studies reporting the benefits of omega-3s. When studies present inconsistent results, both interpretations are plausible. I favor caution in such situations, but not everyone agrees.

Because findings are inconsistent, so is dietary advice about eating fish. The American Heart Association recommends that adults eat fatty fish at least twice a week, but U.S. dietary guidelines say: “Limited evidence suggests an association between consumption of fatty acids in fish and reduced risks of mortality from cardiovascular disease for the general population ... however, more research is needed.” Whether or not fish uniquely protects against heart disease, seafood is a delicious source of many nutrients, and two small servings per week of the less predatory classes of fish are unlikely to cause harm.

Sodas and Obesity

Sugars and corn sweeteners account for a large fraction of the calories in many supermarket foods, and virtually all the calories in drinks—soft, sports and juice—come from added sugars.

In a trend that correlates closely with rising rates of obesity, daily per capita consumption of sweetened beverages has grown by about 200 calories since the early 1980s. Although common sense suggests that this increase might have something to do with weight gain, beverage makers argue that studies cannot prove that sugary drinks alone—independent of calories or other foods in the diet—boost the risk of obesi-

DESIGNER SUPERMARKETS

Marketing experts design nearly every feature of food stores—from product placement to mood music—to maximize sales.

When customers enter a grocery store, the first thing they see is typically something colorful, aromatic and enticing—fresh produce, for example.

The long center aisles and aisle-end displays are jam-packed with products, forcing shoppers to pass by many items that they might purchase on impulse.

Food companies pay supermarkets to get their products—salty chips and other junk foods—positioned prominently in huge displays.

Checkout lines are plastered with candy and other junk food items—the last temptation.

ty. The evidence, they say correctly, is circumstantial. But pediatricians often see obese children in their practices who consume more than 1,000 calories a day from sweetened drinks alone, and several studies indicate that children who habitually consume sugary beverages take in more calories and weigh more than those who do not.

Nevertheless, the effects of sweetened drinks on obesity continue to be subject to interpretation. In 2006, for example, a systematic review funded by independent sources found sweetened drinks to promote obesity in both children and adults. But a review that same year sponsored in part by a beverage trade association concluded that soft drinks have no special role in obesity. The industry-funded researchers criticized existing studies as being short-term and inconclusive, and pointed to studies finding that people lose weight when they substitute sweetened drinks for their usual meals.

These differences imply the need to scrutinize food industry sponsorship of research itself. Although many researchers are offended by suggestions that funding support might affect the way they design or interpret studies, systematic analyses say otherwise. In 2007 in-

vestigators classified studies of the effects of sweetened and other beverages on health according to who had sponsored them. Industry-supported studies were more likely to yield results favorable to the sponsor than those funded by independent sources. Even though scientists may not be able to prove that sweetened drinks cause obesity, it makes sense for anyone interested in losing weight to consume less of them.

The examples I have discussed illustrate why nutrition science seems so controversial. Without improved methods to ensure compliance with dietary regimens, research debates are likely to rage unabated. Opposing points of view and the focus of studies and food advertising on single nutrients rather than on dietary patterns continue to fuel these disputes. While we wait for investigators to find better ways to study nutrition and health, my approach—eat less, move more, eat a largely plant-based diet, and avoid eating too much junk food—makes sense and leaves you plenty of opportunity to enjoy your dinner. ■



Noted nutritionist Marion Nestle discusses genetically modified and irradiated produce and the politics surrounding government dietary guidelines for fruits and vegetables in an excerpt from her book *What To Eat*. Go to www.SciAm.com/ontheweb

WHAT TO EAT: Fruits, vegetables and whole grains constitute the main components of a healthy diet.

MORE TO EXPLORE

Low-Fat Dietary Pattern and Risk of Invasive Breast Cancer: The Women's Health Initiative Randomized Controlled Dietary Modification Trial. Ross L. Prentice et al. in *Journal of the American Medical Association*, Vol. 295, No. 6, pages 629–642; February 8, 2006.

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TRIATHLETES can now top 300 pounds, part of the fat-but-fit movement. The scientific consensus, though, still holds that obesity is unhealthy.

CAN FAT BE FIT?



A well-publicized study and a spate of popular books raise questions about the ill effects of being overweight. Their conclusions are probably wrong

By Paul Raeburn

KEY CONCEPTS

- A much discussed 2005 study showed that people at a “healthy” weight have higher mortality than those who are overweight.
- At about the same time, several popular books—under the banner of fat but fit—derided the notion that being overweight is necessarily unhealthy.
- This challenge to the prevailing orthodoxy continues to provoke ardent debate. But most nutrition experts still warn about the consequences of carrying extra pounds.
- The health-conscious, nutritionists counsel, should use the body mass index based on height and weight as a gauge to judge proper weight. —The Editors

Two years ago Katherine M. Flegal, a researcher at the Centers for Disease Control and Prevention, did a new statistical analysis of national survey data on obesity and came to a startling conclusion: mildly overweight adults had a lower risk of dying than those at so-called healthy weights.

Decades of research and thousands of studies have suggested precisely the opposite: that being even a little overweight is bad and that being obese is worse. The distinction between overweight and obese—which are sometimes both classified under the rubric of obesity—can be confusing. It relates to the measure called body mass index (BMI), derived by dividing one’s weight in kilograms by the square of one’s height in meters. A myriad of Internet-based calculators will handle the math for you. The only thing to remember is that a BMI of at least 25 but less than 30 is considered overweight, and one of 30 or more is characterized as obese.

The long-established conventional wisdom holds that Americans carrying excess fat are at increased risk of death from heart disease, diabetes and various kinds of cancer. And those who do not die of obesity-related ailments can possibly look forward to a variety of other un-

pleasant consequences of their weight, including diabetes and its complications, such as the loss of an arm or leg, blindness and kidney failure. That has been the consensus view of most experts for decades, and it has not changed.

Just as Flegal’s study appeared, a series of books—by lawyers, journalists, political scientists and other academics outside the medical profession—was published, all challenging conventional wisdom on obesity. Fat, the critics said, was not as bad as we had been led to believe. Furthermore, they said, the research community that condemned obesity had a financial stake in that point of view because of the scientists’ complex ties to drugmakers and weight-loss clinics.

The flow of critical books has continued. Earlier this year Barry Glassner, author of the best-selling book *The Culture of Fear* (Basic Books, 2000), published *The Gospel of Food: Everything You Think You Know About Food Is Wrong* (Ecco, 2007). He argues that if we paid more attention to enjoying our food, rather than dieting and counting calories, we would be happier and healthier. It is an appealing argument, but Glassner, a sociologist at the University of Southern California, has not done any research studies to show whether it is true.

The stakes in this debate are high. A major thrust of the nation's disease prevention efforts are aimed at ending what orthodox researchers say is an epidemic of obesity. If being overweight or obese is as harmful as these investigators say, the associated health care costs constitute a substantial drag on the American economy. The CDC estimated in 2004 that obesity's costs in health care and lost productivity amount to \$75 billion annually. Put an end to the fattening of America, these researchers say, and Americans will be healthier, live longer and pay less for their medical care. We might even see gains in American competitiveness, with growth in jobs and wages.

If too much fat is not an important cause of heart disease and other serious illnesses—the possibility raised by Flegal and other critics—then efforts to trim American waistlines are entirely misplaced. Many of the leaders in the obesity research community dismiss the criticism. “It’s complete nonsense, and it’s obviously complete nonsense, and it’s very easy to explain why some people have gone astray,” says Meir Stampfer, a professor of nutrition and epidemiology at the Harvard School of Public Health. Stampfer and his Harvard colleague Walter Willett have done a series of decades-long studies involving hundreds of thousands of people that have laid the foundation for much of what is known about the dangers of being overweight or obese.

Stampfer cites the Flegal study as a prime example of the errors the critics make. The reason being overweight seemed to reduce mortality is because Flegal used the wrong comparison group, he says. The lean group in her study included smokers and people with chronic illnesses—both of whom have increased mortality risks, but not because they are slim. “When you get sick, you lose weight, and you die,” Stampfer says. Compared with those who are smokers or chronically ill, people who are overweight come out looking better than they should.

Willett points to a November 2006 study by James A. Greenberg, a researcher at Brooklyn College, to prove his point. Greenberg performed a similar statistical analysis to Flegal's, this time adjusting for factors such as a history of serious illness. When he did, the number of extra deaths for the obese—compared to those with a “healthy” weight—tripled. And he found a significant increased mortality risk in those who were merely overweight, contrary to Flegal's finding that being overweight lowered the risk of death.

Flegal has acknowledged that she did not exclude the chronically ill from her study but argued in a follow-up report that she had done further analyses that showed it would not have made a difference. The disagreement turns on subtle statistical arguments. What is clear, however, is that Flegal's paper is one of a handful that contradict many studies that support the conclusion that being overweight is harmful. Flegal is not necessarily wrong, but the preponderance of evidence clearly points in the other direction.

Willett thinks this assertion is simply the latest recycling of the notion that Americans have been somehow duped about the risks of obesity. “About every 10 years this idea comes along that says it’s better to be overweight. And we have to stomp it out,” he says. Willett's research has identified profound advantages to keeping weight down—even below the so-called healthy levels.

Many Americans find it difficult to get under a BMI of 25, the border between the overweight and healthy groups. But Willett's work suggests that losing more weight is even better. To take one example, people with a BMI of 20 who gain enough to reach a BMI of 25 have quadrupled their risk of diabetes, Willett says. “If they go up over a BMI of 30, they’ve increased their risk of diabetes 30- to 60-fold,” he says. “And diabetes is not a good thing to have.”

So, in light of conflicting evidence, what is the state-of-the-art summary of the conventional wisdom? Willett puts it this way: keep an eye on three numbers. One is your BMI—keep it within the normal range (20 to 24.9), and preferably near the low end of that range. The second is your weight change after age 20. Although obesity has become increasingly common in children, most people who are now adults were probably close to their proper weight when they were 20, he says. Try to get back to that. The third number is waist circumference—if your belt size has increased since you were 20, that is something to reverse, too.

The consequences of working on these three numbers, he says, will be “huge benefits in health.” But even small reductions in weight are beneficial. “If people can lose 5 to 10 percent of their weight, they will have done themselves a huge favor. If they can take another step, another 5 to 10 percent, they will have done themselves another favor.” Some of the details have changed—but that is the same advice obesity experts have been dispensing for years. ■

[THE AUTHOR]



Paul Raeburn writes about science, policy and the environment from New York City. This former science editor and senior writer for *Business Week* is also a commentator for National Public Radio and a past president of the National Association of Science Writers.

➔ MORE TO EXPLORE

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WHAT FUELS FAT

The human body's ability to store energy as fat seems haywire in a world full of food. Understanding how our complex energy-regulating systems can falter and lead to obesity is revealing new ways to fight excess weight

KEY CONCEPTS

- Our bodies' ability to stockpile energy for future use was critical to survival when food was scarce. Now, in a world of plenty, obesity is the life-threatening problem for an increasing number of people.
- Scientists are working to understand the mechanisms the human body uses to regulate its storage of energy in the form of fat, as well as how these systems can become unbalanced and lead to obesity.
- As the components of this regulatory system are identified, they are providing new targets for drug treatments that could restore energy balance and help to reverse obesity.

—The Editors

By Jeffrey S. Flier & Eleftheria Maratos-Flier

At the dawn of humanity, and for much of our history since, meals were literally catch-as-catch-can. Because humans evolved in a world where food was available only intermittently, survival required that we have the capacity to store ingested energy for times when none was around. Adipose tissue, familiarly known as fat, is the organ specialized for that task.

Our ability to store fat remains essential to life and can allow a person to survive starvation for several months. In very recent human history, however, the amount of energy packed away as fat has been increasing in many populations. When fat storage approaches a level that compromises a person's health, we call it obesity.

In part, this trend is the result of humanity's technological progress—in the face of abundant food and a reduced need for physical activity, it is all too easy to take in more energy than one needs. Yet some people seem to be more susceptible than others to becoming obese when exposed to this plentiful environment, which suggests that variations in individual physiology

may also be influencing how much energy a person consumes, expends and stores as fat.

Many critical variables within the body, such as blood pressure, body temperature, blood sugar and water balance, are tightly controlled by automatic mechanisms, but whether body weight is similarly regulated has long been the subject of vigorous debate. Scientists have only recently begun to make significant advances in identifying pathways of cellular signaling and activity that might participate in such a regulatory system for fat.

These new insights into how the body senses and responds to its energy needs and stores are helping researchers to understand how inherited genetic variations can subtly or powerfully affect those mechanisms and how they can also be upset by environmental influences as well as by excess fat itself. As the discoveries accumulate, scientists gain a clearer picture of the complex physiological systems involved in controlling fat accumulation and new targets for interventions that could help individuals attain greater control in their own battles against bulge.



Consequences of having no regulatory system for controlling body weight would be substantial.

Is There a Fat-o-Stat?

Any system of physiological regulation requires a way for the body to sense the quantity of a specific substance present and to translate that information into actions that keep that variable within a desired range. The moment-to-moment energy needs of human cells, for example, are met by glucose, derived from food, circulating in the bloodstream. Normally the body keeps glucose levels within very tight limits. When blood glucose rises, specialized cells in the pancreas detect the change and secrete extra insulin, which triggers responses in muscle and adipose that cause those tissues to take in and utilize more glucose, while the liver responds by decreasing its own glucose production.

The adipose cells convert the excess energy they have taken in to triglyceride, a fatty acid. When food is not available and insulin levels fall, the fat cells release triglycerides back into the bloodstream, where they are transported to the liver and broken down into ketones, which can serve as fuel for muscle and the brain.

Studies of both animals and humans have long suggested that the mammalian body has mechanisms for monitoring the amount of energy it has stored as fat and for regulating that resource to remain near a particular level. If an animal has been at a stable weight, for example, significantly altering its energy intake will produce physical and behavioral changes that appear to be geared toward restoring weight to the previous level. An animal whose food is suddenly restricted tends to reduce its energy expenditure both by being less active and by slowing energy use in cells, thereby limiting weight loss. It also experiences increased hunger so that once the restriction ends, it will eat more than its prior norm until the earlier weight is attained. Likewise, after intentional overfeeding, an animal will start to expend more energy and exhibit reduced appetite, with both states persisting until weight falls to the previous level.

The consequences of having no regulatory system for controlling body weight would be substantial. Just a 1 percent excess of energy consumption over expenditure, for instance, could cause an average-size man to gain 60 pounds over 30 years. But do humans have an active system that maintains our stored energy balance, analogous to the mechanisms that control circulating glucose levels? The answer is yes. Though imperfect, such a system does exist and investigators, including our respective research groups, are making encouraging

progress toward identifying its components.

As the pieces of this puzzle come together, a general observation can be made that may disappoint but will probably not surprise anyone who has struggled to lose weight: the human body's regulation mechanisms seem to be slightly biased in favor of preserving fat rather than eliminating it. In light of fat's value to survival, this tendency makes evolutionary sense. Over time, evolution could even have favored slight variations in relevant genes that produced the "thriftiest" management of precious energy stores.

Differences in obesity susceptibility among subgroups of people can also sometimes be tied to differing versions of particular genes. Very recently, for example, genome-wide scans performed on nearly 40,000 study subjects around the world identified a gene called *FTO* whose variation was linked to obesity. In every country studied, carriers of one version of the *FTO* gene were on average three kilograms heavier than others in their population and had nearly double the risk for becoming obese. At this point, the function of the *FTO* gene and how it might promote obesity are completely unknown, but its association with increased body weight suggests that it might have a role in weight regulation.

Genes do not function in a vacuum, however, and the genes of the human population in general have not changed over the past few decades. Explaining the relatively recent epidemic of obesity will therefore require a much better understanding of how variant genes interact with a person's environment to influence body weight as well. Some important environmental factors are obvious, such as the reduced need for physical exertion to survive and the increased quantity and quality of available food. Many other environmental variables are less self-evident and still poorly comprehended, such as the effect of nutrition during fetal development on body weight in later life. Stress, sleep deprivation and even viral infections and the composition of benign microbial communities within the body are additional factors that may affect an individual's fat regulation.

Identifying the genes that are normally involved in the body's management of fat is nonetheless allowing researchers to clarify some of the fundamental mechanisms at work. Not surprisingly, following the trail of protein signals encoded by those genes often leads to the master command center for many physiological processes, the brain.

[THE AUTHORS]



Jeffrey S. Flier and **Eleftheria Maratos-Flier** are husband and wife, and each heads a laboratory within the division of Endocrinology, Diabetes and Metabolism at Beth Israel Deaconess Medical Center in Boston. Both are professors of medicine at Harvard Medical School, and Flier became dean of that school on September 1. The authors investigate the physiology of obesity and diabetes, and each has uncovered key components of the systems that regulate the body's energy balance. Flier is especially interested in the functions of leptin and insulin, both in health and disease, and Maratos-Flier has characterized the multiple roles of melanin-concentrating hormone. Recently, she also identified the critical part played by a liver protein in triggering fat cells to release stored energy.

COMMAND CENTER

The human brain regulates weight by integrating information about the body's energy needs and the status of its stores, then initiating changes in behavior and energy processing in response. Specialized brain areas stimulate feelings of appetite or satiety to cause more energy, in the form of food, to be taken in or to terminate a meal. Over time, the brain can also raise or lower the body's overall energy use and reallocate energy away from systems, such as reproduction, that are not essential for short-term survival.

INFORMATION

STORED ENERGY STATUS

- Circulating leptin, a hormone generated by fat cells, indicates how much fat they contain

METABOLIC STATUS

- Circulating glucose represents energy immediately available to cells
- Various indicators of liver activity signal that ingested energy is being processed

FEEDING STATUS

- Neural and chemical signals from the gut indicate whether digestive organs are full of food

RESPONSES

ALTER BODY'S ENERGY INTAKE

- Direct meal timing and size through appetite and satiety signals

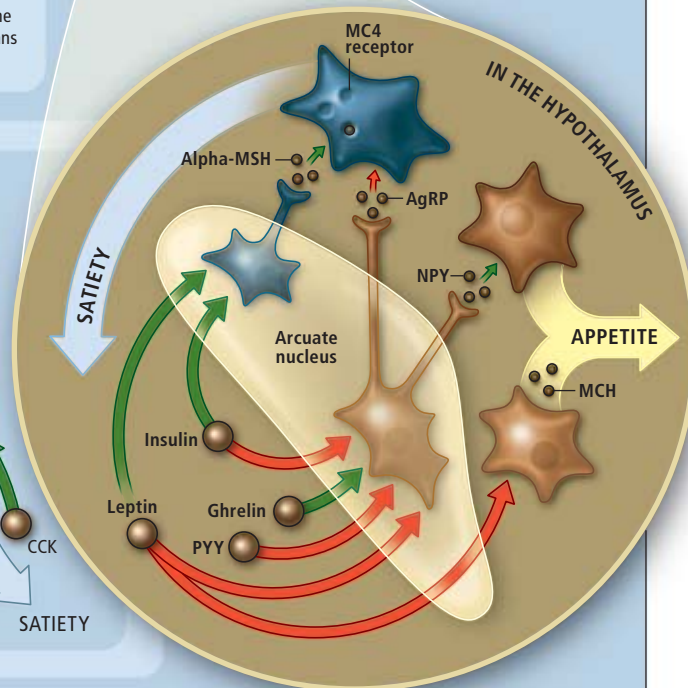
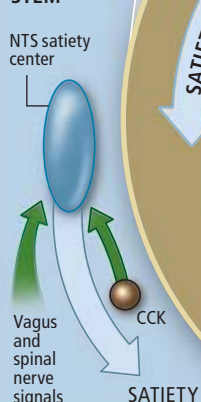
ALTER BODY'S ENERGY USE

- Reduce or increase physical activity
- Slow or speed cellular energy use
- Suppress or restore growth, reproduction and immune function

APPETITE CONTROL

In the arcuate nucleus (ARC) of the hypothalamus (*far right*), indicators of energy and feeding status in the form of gut peptides such as ghrelin and PYY, and hormones including leptin and insulin, act upon groups of neurons associated with appetite (*brown*) or satiety (*blue*). Each substance either stimulates (*green arrows*) or dampens (*red arrows*) the neurons' responses. When stimulated, the ARC cells release peptides such as NPY, AgRP and alpha-MSH, which act on a second set of hypothalamic neurons that induce appetite or satiety. Leptin and insulin act through both types of cells simultaneously to promote satiety while suppressing appetite. Nerve signals and the gut peptide cholecystokinin (CCK) also communicate feeding status directly to the nucleus tractus solitarius (NTS), a satiety center (*right*) in the brain stem.

IN THE BRAIN STEM



Information Integration

Very little happens anywhere in the human body without the brain playing a part by monitoring the situation and exerting its influence. The brain can thus be expected to have a critical role in regulating weight through its direction of appetite, motivation and physical activity, as well as its management of how energy is allocated within the body.

Indeed, a small region at the base of the brain called the hypothalamus has been known for many years to be central to these energy-regulating activities. In animal studies, placing tiny lesions in this area can cause obesity or leanness depending on their precise location. Such observations have led to certain parts of the hypothalamus being labeled as “satiety” or “feeding” centers.

By stimulating appetite or the feeling of satiety, the brain can directly manage the body's energy balance from day to day. Over longer periods, signaling from the brain can also suppress nonessential systems, such as growth and reproduction, when fat stores are too low and energy must be conserved for survival. For the brain to command any of these mechanisms in response to the body's needs, however, it must receive updated information about how much stored energy is available.

What might this signal be, and how might it work? Many different molecules have been shown to influence appetite as their levels in the bloodstream rise and fall, including various breakdown products of food, such as glucose, and gut-derived hormones, such as insulin and cholecystokinin (CCK). But a critical regulator

MIXED MESSAGES

Important signals that stimulate energy-regulating responses by the brain and tissues of the body emanate from digestive organs and from fat itself. They constitute both short-term indicators of the body's feeding status, such as nerve impulses and secreted peptides generated just before and after meals, as well as longer-term information about the status of the body's stored energy. In addition to leptin, which reports body fat levels to the brain, fat cells secrete nearly a dozen other hormones—collectively known as adipokines. At least two of these directly alter tissue responses to insulin, which regulates how much glucose cells take in and use as fuel.

EMPTY STOMACH

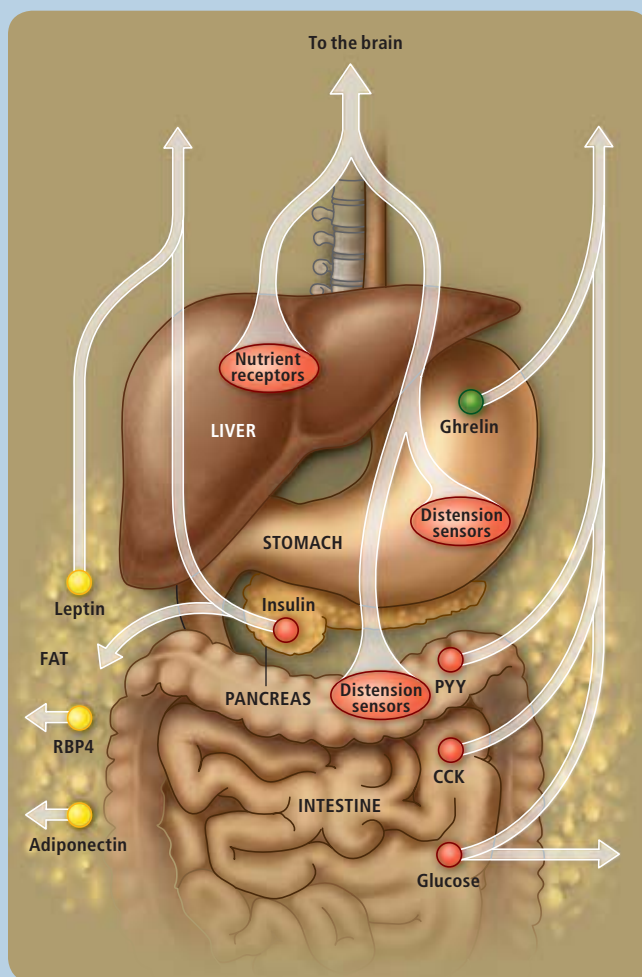
- Ghrelin is produced by glands in the stomach 20 to 30 minutes before eating. The trigger for its release is unclear, but ghrelin may signal the stomach's readiness for a meal to the brain

FULL OF FOOD

- Stomach and intestinal distension is transmitted via spinal and vagus nerves to the brain
- Nutrient receptors in the liver also send neural signals indicating that ingested food is being broken down
- Circulating levels of insulin, secreted from the pancreas, and glucose, derived from ingested food, reflect feeding status and readily available energy
- Cholecystokinin (CCK) and PYY are peptides manufactured by the intestines and secreted into the bloodstream after a meal

STORED ENERGY

- Leptin is manufactured by adipose tissue in amounts proportionate to the fat it contains
- Secreted retinol-binding protein 4 (RBP4) also rises with fat levels and reduces other tissues' responsiveness to insulin
- Adiponectin enhances cellular responses to glucose and insulin, but this adipokine's levels fall in obesity



Discovery of leptin opened the door to exploration of a whole new biological pathway.

of how much energy is maintained in storage proved elusive until Jeffrey Friedman of the Rockefeller University and his colleagues discovered leptin in 1994.

Decades earlier a spontaneous syndrome of severe obesity with increased appetite and decreased energy expenditure appeared in certain mice bred at the Jackson Laboratory in Maine. Because a mouse had to inherit the trait from

both parents, the syndrome itself was called ob/ob. Despite hundreds of studies attempting to understand obesity in these mice, Friedman's group was the first to identify the inherited gene mutation responsible. The researchers also determined that the newly identified gene was predominantly active in fat cells and gave rise to a protein that was not made in functional form in the mice harboring the ob mutation. The obesity

syndrome seemed to be caused by the absence of this substance.

The researchers named the protein leptin, from the Greek root *leptos*, for “thin,” and quickly demonstrated that replacing the missing leptin by daily injections lowered the weight of affected mice by reducing their appetite and increasing their energy expenditure. Very soon, others furthered this remarkable discovery by finding a similar loss-of-function mutation in the human leptin gene among people with extremely rare cases of severe, early-onset obesity. Administering leptin to these subjects helped them to lose weight just as it had the mice.

These experiments demonstrated for the first time a physiological system whereby fat cells produce a hormonal signal that reflects their state of energy storage—the more triglyceride a fat cell contains, the more leptin it generates—and to which the brain responds by altering appetite and energy expenditure. When this energy-status signal is absent, either because the genetic mutation prevents functional leptin proteins from being manufactured or because the body actually has low fat stores, the brain believes that the body is starving and behaves accordingly by promoting hunger and energy conservation.

The discovery of leptin opened the door to exploration of a whole new biological pathway of cellular signaling and responses. The brain was clearly a major target of leptin secreted into the bloodstream by fat cells, and researchers, including ourselves, have begun to learn many of the detailed neural circuits and cell types through which leptin acts. As might be expected, many of them are in the hypothalamus [see illustration on page 75].

In a structure called the arcuate nucleus of the hypothalamus, within the area previously identified as a satiety center, leptin simultaneously affects two neighboring neuron populations that control appetite in opposite ways. One set of neural cells produces a peptide called alpha-MSH that reduces appetite and, consequently, body weight. The other set of neurons produces two neuropeptides, NPY and AgRP, both of which stimulate feeding and promote obesity. Leptin’s interactions with both these cell groups are quite elegant. Neurons that produce MSH connect to neurons elsewhere in the hypothalamus that carry a surface protein known as the melanocortin 4 receptor (MC4R), whose activation reduces appetite and promotes weight loss. AgRP, the peptide that promotes feeding, is an antagonist of this receptor, meaning that it

prevents receptor activation. Thus, leptin acts to trigger MC4 receptors both by stimulating them directly via the MSH-producing neurons and by inhibiting their antagonist.

At the same time, leptin also affects the brain area previously viewed as a feeding center, the lateral hypothalamus, in an interesting way. One group of cells in that region produces a small protein called melanin-concentrating hormone (MCH). In 1996 our research group discovered that levels of this peptide are raised in the ob/ob mouse type, suggesting that leptin normally inhibits production of the peptide. We also established that increased MCH promotes food intake and obesity and found that even ob/ob mice, if they lack the ability to manufacture MCH, are substantially less obese. We had thus found another clear example of the physiological system through which leptin acts as a signal that regulates hypothalamic neuropeptides, which in turn exert control over appetite and energy balance.

The same cells and circuits affected by leptin, moreover, are also acted on by numerous other circulating factors. The hypothalamus and related brain areas integrate all this information coming from diverse sources to produce a real-time picture of the body’s energy status and orchestrate responses to manage energy resources. For a better understanding of what these signals, including leptin, are telling the brain, researchers are also studying how and where they originate.

Visceral Responses

A full belly is a simple but sure sign that the body has recently taken in energy as food, and stomach distension has long been known to reduce appetite. One way that this physical state is communicated to the brain is via distension-sensitive nerve fibers that carry signals from the stomach and intestine, ultimately reaching appetite-control centers. Neural signals reflecting the energy-processing state of the liver may also be transmitted to the brain via the vagus nerve.

Insulin is also believed to act directly on neurons in the hypothalamus to suppress appetite, and several other hormones manufactured in the intestine and released into the bloodstream after meals are known to travel to the brain and produce the same effect. Among these, cholecystokinin is an important factor in causing short-term satiety, but its actions are limited to signaling termination of individual meals. Another peptide called PYY, released from the small intestine, does the same.

HUNGRY HELPERS

A person’s internal “environment” might influence how much of a meal gets turned into body fat. Trillions of benign microbes inhabit the human gut, helping to break down food, but the mix of species residing in different individuals can vary. Researchers at Washington University in St. Louis have shown that in obese people, a division of bacteria known as firmicutes predominates, whereas bugs from the division bacteroidetes are more populous in lean individuals. Moreover, the “fat” microbe set has the ability to extract more nutrients, hence calories, from food than the lean set. Whether the difference in microbiota is a contributor to obesity, a consequence, or both, remains to be determined.



FRIENDLY FIRMICUTES:
Lactobacillus fermentum

So far only one gut-generated peptide that acts to spur appetite has been identified: ghrelin is made and released in the stomach before feeding and may signal anticipation of a meal [see illustration on page 76].

In people who are already obese, it is possible that dysfunctional generation of such short-term signals indicating whether food has recently been consumed, or is about to be, could skew the brain's energy-regulation mechanisms. Losing as little as 10 pounds, for example, can cause ghrelin output to rise, provoking increased hunger.

Over the long term, signals emanating from body fat itself might also contribute to abnormal energy management. For many years, fat was viewed primarily or exclusively as a passive site for energy storage and release in the form of fatty acids, but with the discovery of leptin, adipose tissue was recognized as an endocrine gland whose activity has widespread effects on health [see box on opposite page].

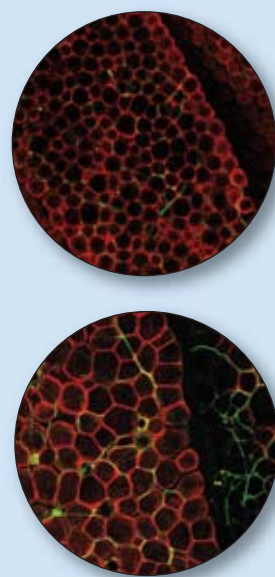
Leptin is still the only fat-derived hormone conclusively shown to participate directly in regulation of fat stores, but a group of others, often collectively referred to as adipokines, are under investigation as well. Adiponectin, for example, is a molecule produced and secreted exclusively by fat cells that normally circulates in the bloodstream in high concentrations. Adiponectin levels are lower than average in obese subjects for unknown reasons, and experimental mice lacking adiponectin are extremely heavy, although the mechanism underlying this effect is also mysterious. Some intriguing research suggests that under certain circumstances adiponectin might have a direct appetite-stimulating effect in the brain. Although such findings are very preliminary, they point to the possibility that adiponectin, too, could serve as a direct signal from fat cells to the brain indicating a need to take in energy. As such, it might offset leptin's appetite-suppressing role in energy regulation.

Origins of Obesity

Much remains to be discovered about the extremely complex circuitry regulating the body's energy use and storage as well as how disruptions within it might help perpetuate existing obesity or predispose an individual to becoming obese in the first place. The discovery of leptin in mice led to the identification of a few humans whose severe obesity could be explained by a single genetic defect. Such "monogenic" obesities are quite rare but very informative. For example, a handful of patients have been identi-

SELF-REGULATING CELLS?

In obesity, overstuffed fat cells excrete more leptin, a signal of abundant energy stores to which the brain responds by cutting appetite. But do fat cells also put out calls for more energy when they are running low? Research published in July indicates that another hormone generated by fat cells, adiponectin, might play that role. Takashi Kadowaki and his colleagues at the University of Tokyo showed that in mice, fasting raises adiponectin levels in spinal fluid and the hormone's presence in the central nervous system triggers the brain's release of the appetite-stimulating peptide NPY. If adiponectin is confirmed to be a starvation signal, to which the brain responds by increasing food intake, then it would represent the second fat-generated molecule directly involved in regulating fat stores.



FAT CELLS in lean (top) and obese (bottom) mice.

fied with severe obesity attributable to mutations in the genes for leptin, the leptin receptor, or POMC, a precursor of the appetite-depressing hypothalamic peptide MSH.

Mutations that cause loss of functioning MC4 receptors—the targets of MSH—are also very important, accounting for between 3 and 5 percent of patients with severe obesity. In most of those individuals, only one of two copies of the gene is affected, leaving them with about 50 percent of normal MC4 receptor function.

The majority of people with obesity, however, have no known genetic mutations that could explain their condition. Moreover, their leptin levels are actually higher than those of lean individuals, which sounds counterintuitive if leptin is supposed to cause appetite suppression. Indeed, this discovery led to the idea that most obese patients may have leptin resistance—for some reason, leptin's signal that fat stores are abundant is not being heard by some part of the energy-regulation pathway. Consistent with this theory is the fact that attempts to administer leptin therapeutically have produced disappointingly poor responses in typical obese patients lacking specific leptin-associated gene mutations.

Finding the molecular basis for leptin resistance is therefore a matter of substantial research interest. Two proteins have been implicated strongly as contributing to leptin resistance by acting in the brain and possibly in peripheral tissues. One is called SOCS3 and is produced by hypothalamic neurons that normally respond to leptin. SOCS3 can block leptin's ability to signal to those cells. The other protein, PTP1B, squelches leptin signaling inside the cells. In mouse experiments, reducing levels of SOCS3 or PTP1B in all tissues, or even just in neurons, makes mice more sensitive to leptin and resistant to obesity. The precise role of these proteins in human leptin resistance is still unknown, but based on these observations in animals it is tempting to speculate that such molecules produced by leptin-sensitive neurons serve the purpose of modulating leptin signaling so that the cells do not become overwhelmed by it. In obese individuals, chronically high leptin levels could therefore cause these proteins to start overcompensating to protect the cells, initiating a cycle of increasing resistance to leptin signaling.

Such physiological feedback mechanisms could help perpetuate and worsen obesity, and variations in genes involved in fat-regulating pathways may have a similar role in unbalancing the system. Indeed, we believe that varia-

Fat's Fuzzy Role in Disease

A clear association between obesity and a variety of serious illnesses, including diabetes, hypertension, cardiovascular disease and even cancer, has been established, although many aspects of the relation between fat and illness are still unexplained. The most common medical definition of obesity is nonetheless based on evidence of adverse health effects in people above certain weights. The body mass index (BMI) is calculated as a person's weight in kilograms divided by height in meters squared. Because higher mortality is seen at BMIs greater than 30, that number has become the accepted cut-off for obesity. A BMI between 25 and 30 is called overweight, reflecting some connection with adverse health effects.

These epidemiological relations between BMI and illness can vary in different subpopulations, however. And no precise number can allow doctors to determine what amount of excess fat will cause illness in a given patient. Some people experience health problems at the relatively low BMI of 25, whereas others remain healthy at BMIs higher than 30 [see "Can Fat Be Fit?" by Paul Raeburn, on page 70].

Nor does all fat appear to have equal effects. Adipose tissue accumulates underneath the skin in most body areas, as well as in and around internal organs, especially in the abdomen. Many studies strongly suggest that diabetes and cardiovascular diseases in particular are tightly linked to that intra-abdominal, or visceral, fat. In some cases even significant excess fat in the hips and thighs—producing the proverbial "pear" shape—is relatively unlikely to cause those diseases when excessive abdominal fat is not also present. Conversely, excess abdominal fat is associated with diabetes and other metabolic imbalances, even in the absence of abundant lower-body fat, as in the "apple"-shaped body type.

The basis for the influence of location on fat's health effects is not

fully understood. One theory focuses on the fact that abdominal fat is well placed to release fatty acids and possibly other substances and signals into the portal vein that directly bathes the liver, thereby potentially affecting the functioning of that critical organ. A second theory is based on the fact that fat depots in different parts of the body generate varying amounts of certain chemical signals, and the higher relative volumes emanating from visceral fat may account for its more adverse effects.

Several specific fat-generated signals are also strongly implicated in obesity-related health problems. Adipose tissue produces triggers of inflammation, for example, which could contribute to risk for cancers, cardiovascular disease, diabetes and other immune disorders. The hormone adiponectin, in contrast, has desirable actions in several tissues to improve glucose and lipid processing by cells. Because circulating adiponectin levels fall in obesity, however, the loss of its beneficial effects is associated with the development of insulin resistance, which contributes to diabetes, and vascular disease. A more direct role in insulin resistance is attributed to the adipokine known as retinol-binding protein 4 (RBP4), which fat cells manufacture in greater amounts in obesity. Animal studies show that RBP4 causes liver and other cells to become less sensitive to insulin. A very recent report also confirmed that visceral fat generates greater amounts of RBP4 than subcutaneous adipose tissue elsewhere in the body.

As these few examples illustrate, many of the same molecules and mechanisms under investigation for their role in the body's energy regulation are also involved in other processes vital to health. Advances in understanding obesity will likely result in new insights into obesity-related diseases and their treatment as well.

—J.S.F. and E.M.-F.

APPLES ARE UNHEALTHY when the word refers to body shape. Excess abdominal fat indicates excessive fat packed in and around internal organs, a situation strongly linked to metabolic and cardiovascular disease. In contrast, fat accumulated mainly on hips and thighs, creating a "pear" shape, is less likely to cause illness.



tions in genes that influence body weight through as yet undiscovered mechanisms are a likely source of at least some susceptibility to obesity. Whether there are many such genes whose variation affects weight to a small extent or a few dominant genes whose variation affects weight in most people remains to be seen. With powerful techniques for scanning human genes within large populations becoming more widely available, discovery of new weight-regulatory pathways and new insights into known mechanisms

is bound to accelerate. At present, however, the prevalence of obesity and its complications are continuing to rise, making it clear that highly effective therapies are not yet available.

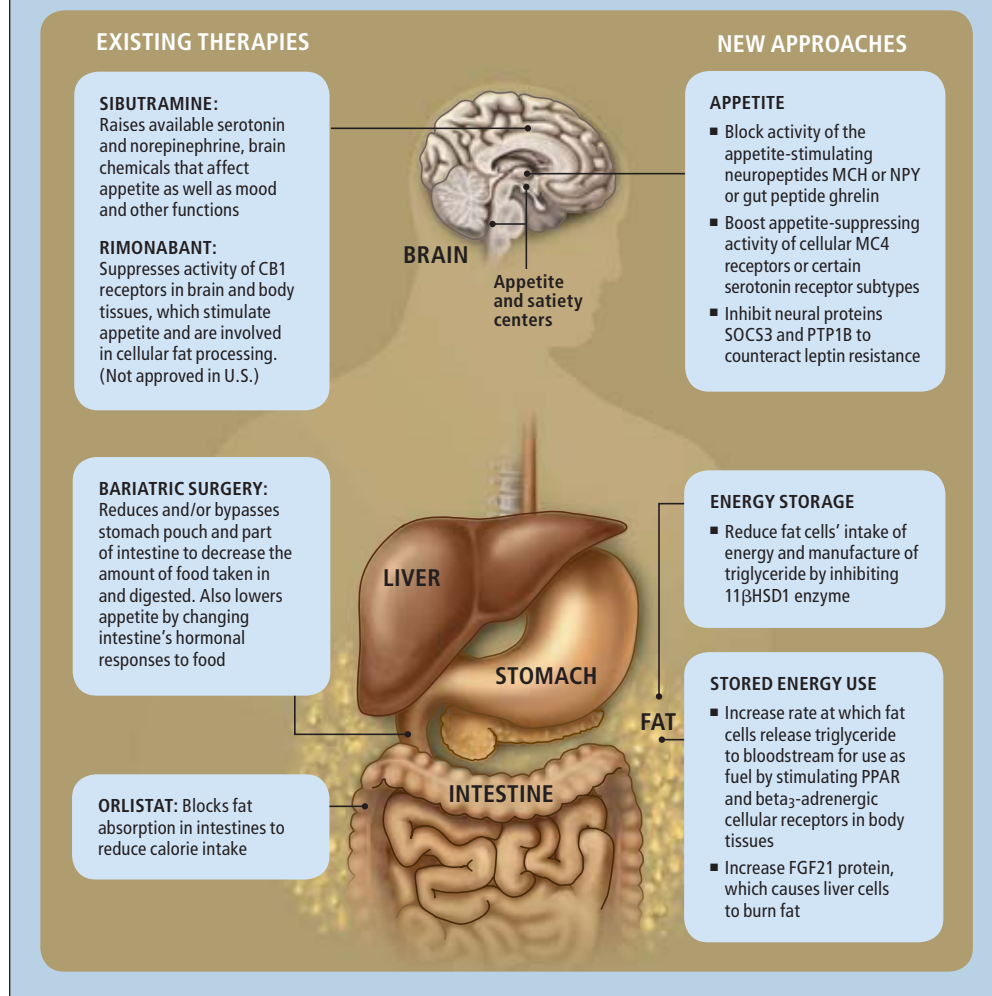
Intervening in Obesity

Simple recommendations such as reducing food intake, changing the composition of one's diet and increasing physical exercise are always appropriate for an obese person. And by themselves, such behavior changes can help individu-

OVERRIDING OBESITY

As the mechanisms that can give rise to obesity become clearer, so do the reasons why losing body fat and keeping it off through behavioral changes alone can be difficult for many individuals. Existing therapies are only modestly effective, and developing new drugs that are safe for prolonged use has been difficult because energy-regulation systems are intertwined with other vital processes in the body and brain, creating a risk of serious side effects. Therapeutic approaches currently in development attempt to more precisely target the molecules and mechanisms that control how much energy the body takes in as food or how much energy it stores and burns.

Successful
therapy
for obesity will
eventually
involve multiple
drugs acting
through
independent
pathways.



als lose up to 10 percent of their body weight, although maintaining that weight loss is often difficult.

Bariatric surgery is now performed on hundreds of thousands of patients every year. In general, these operations either tie off part of the stomach with a band to limit its size or actually reroute the gut to both reduce the stomach pouch and bypass part of the intestine. Both procedures are substantially more successful than any current drug therapies at promoting and maintaining weight loss. Recent research also sug-

gests that gastric bypass may cause a reduction in appetite, in part by altering levels of gut hormones such as ghrelin and PYY, which indicates that drugs to accomplish the same end might someday substitute for these operations in many patients.

Any new drug to treat obesity will be held to very high standards of efficacy, tolerability and safety. Because the pathways regulating energy storage are so critical to other processes in the body and brain, developing drug interventions that meet all those criteria is challenging. Unfor-

fortunate experiences with past drug candidates that were effective but ultimately proved to be addictive or unsafe could in fact push regulatory agencies to be even more demanding than may seem reasonable. In addition to treating obesity by reducing body fat content, a drug will have to improve obesity-associated complications, such as diabetes and hypertension, or at least not cause them to become worse. Any therapy will also have to be safe for extended use because stopping treatment would likely allow weight to return to previous levels. A high risk exists as well for obesity drugs to be misused by people seeking inappropriately low body weights for nonmedical reasons.

Just recently, a new medication that has been available in Europe for some time, rimonabant, failed to gain approval from U.S. Food and Drug Administration advisers because of concern about increased incidence of depression and anxiety in people taking it. The drug works by blocking activation of a cell-surface receptor in the brain and peripheral tissues known as CB1. This receptor mediates the “munchies” brought on by smoking marijuana, as well as the actions of lipid molecules made in various tissues. The trade-offs between safety and efficacy in using this class of compounds over an extended period are therefore not yet clear.

At present, only two prescription drugs are approved in the U.S. for long-term use to treat obesity. Sibutramine, available since 1997, acts to prolong the exposure of neurons in the brain to the neurotransmitters norepinephrine and serotonin, resulting in reduced appetite and modest weight loss. This drug’s use is limited by the fact that blood pressure and pulse tend to rise rather than fall during therapy. Orlistat, available since 1999 and now offered in an over-the-counter form under the brand name alli, lowers an individual’s total calorie intake by acting in the gut to reduce fat absorption, with modest effects on weight and obesity complications.

Many other approaches to the development of obesity drugs are being pursued based on the numerous pathways for regulating appetite and weight that have been discovered in recent years. Potential therapies include inhibitors of the appetite-stimulating molecules MCH, NPY and ghrelin, appetite-suppressing mimics of PYY, and activators of the melanocortin 4 and serotonin receptor subtypes. Any of those options would be targeted toward lowering energy intake, as the existing drugs do. But because the body tends to compensate for fat loss by going

into energy-conservation mode, complementary drugs that boost the rate at which energy is expended might also be necessary.

Several research groups are looking into ways of increasing the rate at which fat cells release stored energy or of preventing its storage from taking place. One approach focuses on stimulating a class of cell-surface receptors—known as beta₃-adrenergic receptors and PPAR nuclear receptors—which trigger tissues’ release of a substance called uncoupling protein 1. That signal is a call for energy, which is heard by certain fat cells and increases the rate at which they send triglycerides back into the bloodstream. Yet this technique may work only on a special type of fat tissue known as brown adipose, which is abundant in rodents and in newborn human infants, but by adulthood very few brown adipose cells remain in human fat.

Another promising approach involves blocking enzyme activities that promote fat storage. One example, the enzyme 11 beta HSD-1 (11βHSD1), causes the steroid cortisol to be converted from a dormant form to a biologically active one inside adipose and liver cells. This locally active cortisol, in turn, prompts those cells to manufacture more triglyceride. Our laboratory group has shown that experimental mice overproducing 11βHSD1 in their adipose cells also generated excess corticosterone (the mouse version of cortisol) in those cells and grew to be significantly obese. Interestingly, the mice developed abdominal obesity in particular, as well as diabetes, high blood pressure and high blood lipids, a suite of symptoms resembling the human condition known as metabolic syndrome.

Although studies of obese human subjects have yet to produce such a clear-cut association between 11βHSD1 activity and excess fat storage, inhibitors of that enzyme already exist and are in development for use in treating metabolic syndrome. They may prove to be useful interventions for obesity as well.

Many experts believe that successful drug therapy for obesity will eventually involve multiple drugs acting through independent pathways, in combinations tailored to individual patients, as is now the case for treating hypertension and diabetes. Of course, as with other common diseases such as hypertension, it would be preferable to treat people with changes in diet and lifestyle alone. But if that approach fails, and morbid consequences result, safe drug therapies would be no less appropriate for obesity than for other illnesses. ■

MORE TO EXPLORE

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THIS IS YOUR BRAIN ON FOOD

**Neuroimaging reveals a shared basis for
chocoholia and drug addiction**

By Kristin Leutwyler Ozelli

Mounting evidence shows that compulsive eating and drug abuse engage some of the same brain circuits in similar ways, offering a new angle for understanding and treating obesity. In an interview with SCIENTIFIC AMERICAN, Nora D. Volkow, who is director of the National Institute on Drug Abuse (NIDA) and a pioneer in the study of addiction, explains these recent findings.

KEY CONCEPTS

- Food and illicit drugs both trigger brain circuits involved with reward and pleasure. They create conditioned responses that are subsequently evoked by the mere sight of food or drugs or by the environment in which these substances are consumed.
- These responses exist on the most fundamental neurophysiological level. Obese people or drug addicts may be trying to compensate for an abnormal response to dopamine, the neurotransmitter that mediates reward-seeking behavior. This anomaly may cause them to dose themselves continuously with food or drugs.
- A multifaceted strategy is needed to treat addiction: Pharmaceuticals, biofeedback and group therapy all have their place.

—The Editors

Which brain circuits do food and drugs activate in common?

The system in the brain that both food and drugs activate is basically the circuitry that evolved to reward behavior essential to our survival. One reason humans are attracted to food is because it is rewarding and pleasurable. When we experience pleasure, our brains learn to associate the sensation with the conditions that predict it. That memory strengthens as the cycle of predicting, seeking and obtaining pleasure becomes more reliable. In scientific terms, we call this process conditioning.

Drugs are particularly effective as conditioning stimuli, primarily by virtue of their chemical properties. Natural reinforcers, such as food or sex, take longer to activate the reward pathway. Important for both, however, conditioning links a memory not just to a stimulus but to the environment in which it is found and other related cues. That's exactly what nature intended: if the action needed to attain a pleasurable experience were triggered exclusively by the stimulus in question, the conditioned response would be very ineffective indeed. Once you create a conditioned memory, it's just like Pavlov's dogs; the response becomes a reflex. This conditioned response underlies the drive both in drug addiction and compulsive eating.

For this reason, high-calorie foods—particularly foods that are high in fat or sugar—are more likely to trigger compulsive eating. As

hunters, we didn't always succeed at finding something to eat and so high-calorie foods, which pack a lot of energy, offered a survival advantage. In that environment, it was in our best interest to consume as many foods of this type as we could find. So they are very reinforcing. But today when we open up our refrigerators, we have a 100 percent chance of finding food. Our genes have changed little, but in our environment we are surrounded by high-fat, high-sugar foods, which have contributed to the rise in obesity.

What is going on in the brain during cravings?

Had Pavlov been able to see inside his dogs' brains, he would have likely seen an increase in dopamine whenever the animals heard a sound he had previously paired with offerings of meat. Dopamine serves to tell us what's important: unexpected bits of new information we need to pay attention to in order to survive—alerts about sex, food and pleasure, as well as danger and pain. We've documented that when you show people foods to which they've been conditioned, there is an increase in dopamine in the striatum, a brain region involved with reward and behavioral motivation.

Mind you, this increase is just from smelling and looking at the food, because we tell study participants that they will not be able to eat it. And this is the very same neurochemical response that happens when addicts see a video of other people taking drugs or see anything to do with their drug of choice. The message that you get when dopamine is liberated in the striatum is that you need to get into action to achieve a certain goal. It is a powerful motivator. Overcoming these impulses with sheer willpower is extremely hard.

Also in the brains of both drug addicts and obese people, we typically find a reduced number of so-called D2 dopamine receptors in the striatum as compared with nonabusers and nonobese

subjects, respectively. Perhaps these findings reveal that the brain is somehow trying to compensate for repeated surges in dopamine from continued drug or food stimulation. Another possibility is that these individuals naturally have lower numbers of receptors to begin with, which may put them at increased risk for diseases of addiction in general. Interestingly, we found a negative correlation between the availability of D2 receptors in obese individuals and their body mass index (or BMI); in other words, the more obese a person was, the fewer receptors he had.

Are certain people at greater risk for drug or food addictions?

We know from twin studies that approximately 50 percent of the risk for both addiction and obesity is genetic. But the genes involved come into play on many different levels—from differences in the efficiency with which we metabolize certain drugs or foods to differences in our likelihood of engaging in risk-taking or exploratory behaviors to more specific risks, such as the underlying sensitivity of the reward system.

In obesity, some people may be at a greater risk for compulsive eating because they may be overly sensitive to the rewards of food. One study showed that some obese people have increased brain activity in response to mouth, lip and tongue sensations. Likewise, some people are not very efficient at registering or responding to internal signals of satiety, so they are possibly going to be more vulnerable to cravings triggered by food cues in their environment.

Does the overlap between addiction and obesity reveal any new targets for treatment?

There are pharmacological interventions to explore, such as medications that increase the dopamine response in the brain. One exciting development is the recent synthesis and preliminary testing of an orally administered drug that blocks orexin, a peptide that reinforces the “high” associated with drinking alcohol and is thought to regulate feeding. This drug could be extremely helpful in the treatment of aberrant food and drug consumption. Also, because of social stigma, both obesity and drug addiction can lead to a deep sense of isolation, which is very stressful, and so group therapy can help.

Yet another exciting area the NIDA is researching is the use of functional magnetic resonance

imaging (or fMRI) in real time to train people to exercise specific parts of their brains, just like muscles. By this method, Sean Mackey of Stanford University, Christopher deCharms of Omneuron [in Menlo Park, Calif.] and their colleagues have trained healthy subjects and chronic-pain sufferers to control their brain activity to actually modulate their experience of pain. So we are exploring the possibility that you might use this kind of technique to train people to control a region of the brain called the insula, which has been implicated in food and drug cravings. Smokers who have a lesion in the insula after a stroke seem to lose the desire to smoke.

A distinct obstacle to recovery for compulsive eaters is the obvious fact that you have to eat to survive, whereas if you are addicted to an illegal substance, you are in a way protected because the drug is not going to be environmentally available everywhere. One of the therapeutic interventions for drug addicts is to teach them to avoid places associated with their habit. But how do you do that with food? It’s impossible. And these people suffer. In rats, it has been shown that if you give them diets very high in sugar and then administer an opioid antagonist called naloxone, you can trigger a withdrawal that is similar to that in animals given naloxone after repeated injections of morphine. This result indicates that chronic exposure to high-sugar diets generates a physical dependence in these rats. If a similar process happens in humans, then interventions aimed at mitigating withdrawal symptoms may benefit dieters. ■

Kristin Leutwyler Ozelli is a freelance writer based in London.

A patient who observes real-time images of his or her brain activity may be able to alter how neural circuitry functions and gain a measure of control over food and drug cravings.

[THE INTERVIEWEE]

Nora D. Volkow is director of the National Institute of Drug Abuse. Before her appointment in 2003, she held various positions at Brookhaven National Laboratory and also served as professor of psychiatry and associate dean for the medical school at Stony Brook University. In her research, she was first to use imaging technology to investigate neurochemical changes associated with addiction.



THE WORLD IS FAT

More people in the developing world are now overweight than hungry. How can the poorest countries fight obesity?

KEY CONCEPTS

- As globalization arrives in the Third World, so does the unhealthy Western diet. Over the past 20 years, poor people in developing countries have greatly increased their consumption of sweetened beverages, vegetable oils and animal-source foods (meat, poultry, fish, eggs and dairy products).
- People in the developing world are also adopting Western lifestyles that contribute to obesity.
- No country in modern times has successfully reduced its number of overweight citizens, but governments and aid programs are considering various interventions.

—The Editors

By Barry M. Popkin

Over the past 20 years a dramatic transition has altered the diet and health of hundreds of millions of people across the Third World. For most developing nations, obesity has emerged as a more serious health threat than hunger. In countries such as Mexico, Egypt and South Africa, more than half the adults are either overweight (possessing a body mass index, or BMI, of 25 or higher) or obese (possessing a BMI of 30 or higher). In virtually all of Latin America and much of the Middle East and North Africa, at least one out of four adults is overweight. Although undernutrition and famine remain significant problems in sub-Saharan Africa and South Asia, even desperately poor countries such as Nigeria and Uganda are wrestling with the dilemma of obesity. Worldwide, more than 1.3 billion people are overweight, whereas only about 800 million are

underweight—and these statistics are diverging rapidly.

The obesity rates in many developing countries now rival those in the U.S. and other high-income nations. What is more, the shift from undernutrition to overnutrition—often called the nutrition transition—has occurred in less than a generation. When I return to villages that I visited 15 years ago in India, China, Mexico and the Philippines, I see enormous changes: kids guzzle soft drinks and watch television, adults ride mopeds instead of walking and buy their food from supermarkets. In addition to adopting more sedentary lifestyles, people in the developing world are also consuming more caloric sweeteners, vegetable oils and animal-source foods (meat, poultry, fish, eggs and dairy products). The combination of lifestyle and dietary changes has paved the way for a public



health catastrophe, with obesity leading to an explosive upsurge in diabetes, heart disease and other illnesses.

To combat this threat, we must look behind the vast social, economic and technological trends that are transforming the Third World. This examination reveals that many governments and industries are contributing to the growth in obesity by flooding developing countries with cheap sweeteners, oils and meat while doing nothing to promote the consumption of fruits and vegetables. Revamping agricultural subsidies and regulating food advertising may help alleviate the damage. But the effort will require new policy research, long-term funding commitments and a hefty amount of political will.

A Problem of the Poor

Mexico is perhaps the most striking example of a developing nation suffering from the obesity epidemic. In 1989 fewer than 10 percent of Mexicans were overweight. In fact, no one in the country even talked about obesity back then; the focus was on poverty and hunger. But national surveys conducted in 2006 found that 71 percent of Mexican women and 66 percent of Mex-

ican men were overweight or obese—figures that approximate those in the U.S. And the health effects are already becoming apparent. Diabetes was almost nonexistent in Mexico 15 years ago, but today almost one seventh of the country's people suffer from type 2 (adult-onset) diabetes, and the disease is spreading quickly.

How could such a radical change have taken place in less than 20 years? Proximity to the U.S. may have exacerbated the problem—many Mexicans are exposed to American culture and media, which could have influenced their dietary or lifestyle choices—but obesity has also burgeoned in countries that have much less contact with the U.S. The migration of people from the countryside to the cities may have also played a role. Studies of more than 157,000 women in 39 developing nations have shown that in nearly all the countries, women in urban areas are more likely to be overweight than women in rural areas. (Researchers have collected more data for women than for men in these studies because their focus was on reproductive health.) But the prevalence of obesity has grown in rural regions, too; for example, in Mexico, Colombia, Turkey, South Africa and



Percentage of adults who are overweight or obese:
20.0 (1975) 36.7 (1997)

Supermarkets have proliferated across Brazil and other Latin American nations over the past two decades, leading to a large rise in the consumption of processed foods.

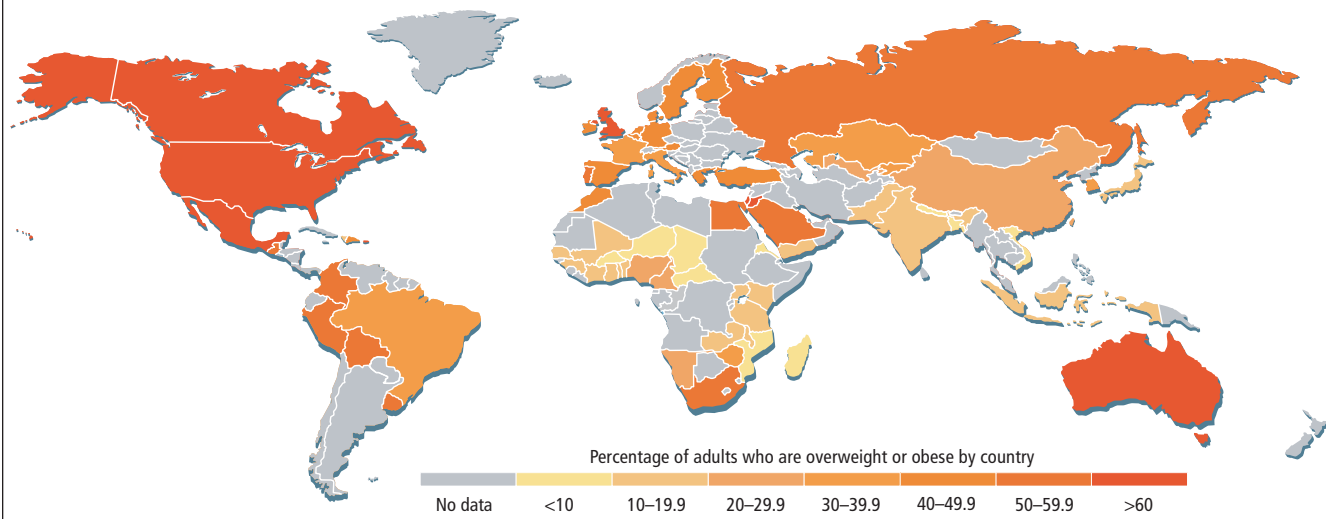


AP/GETTY IMAGES (photograph)

OBESITY SPREADS ACROSS THE GLOBE

People who are overweight (possessing a body mass index, or BMI, of 25 or higher) or obese (a BMI of 30 or higher) are now just as common in many developing countries as they are in the U.S., Canada and Europe. In large

parts of Latin America, North Africa and the Middle East, the problem has triggered an upsurge in diabetes, heart disease and other illnesses. Obesity rates are also rising quickly in China, India and other Asian nations.



Jordan, more than half the rural women are overweight.

A better explanation lies in the connection between obesity and poverty. In the developing world, obesity has become predominantly a problem of the poor, just as it is in the U.S. In all countries with a gross domestic product greater than \$2,500 per capita—which includes most developing nations outside of sub-Saharan Africa—obesity rates are higher for poor women than for those with higher socioeconomic status. As average incomes in these countries have risen, farm laborers and the urban poor have adopted modern habits associated with obesity, such as watching television and shopping in supermarkets, but still do not have access to education, healthier foods or recreational activities that would help them control their weight.

Compounding the tragedy is the fact that obese people in the Third World may be more likely to develop diabetes or high blood pressure than obese individuals of European descent. Scientists have long hypothesized that Latin American, African and South Asian populations may carry a disproportionate number of “thrifty genes” that evolved to help them survive times of famine by enabling them to store fat more efficiently. Unfortunately, when a person with these genes becomes overweight, body fat tends to accumulate around the heart and liver, increasing the risk of diabetes and cardiovascular problems. In China, where obesity levels are

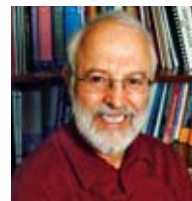
climbing rapidly, nearly one third of the population suffers from high blood pressure. Moreover, I have found in my surveys that only a small fraction of Chinese with hypertension receive treatment for the condition. Whereas Western countries can afford to monitor and provide drugs for diabetic and hypertensive patients, the illnesses go mostly untreated in the developing world, and so health complications appear early on.

A Dietary Disaster

One of the biggest contributors to the obesity epidemic in the Third World is the recent popularity of sweetened beverages. For most of our evolutionary history, the only beverages humans consumed were breast milk after birth and water after weaning. Because water has no calories, the human body did not evolve to reduce food intake to compensate for beverage consumption. As a result, when people drink any beverage except water their total calorie consumption rises, because they usually continue to eat the same amount of food. Although humans have been drinking wine, beer, fruit juice and milk from domesticated animals for thousands of years, the proportion of calories coming from beverages has been relatively small until the past 50 years, when Coca-Cola, Pepsi and other soft drinks began spreading across the globe.

For physicists, a calorie is the amount of heat energy needed to raise the temperature of one gram of water by one degree Celsius. The calo-

[THE AUTHOR]



Barry M. Popkin is a professor of nutrition epidemiology at the University of North Carolina at Chapel Hill, where he directs the Interdisciplinary Center for Obesity. His research program includes large nationwide surveys that have tracked changes in diet, activity patterns and body composition in the U.S., China, Russia, the Philippines, Brazil and other countries. He chairs the Nutrition Transition Committee for the International Union for the Nutritional Sciences and has published more than 260 journal articles, as well as many books. In 1998 he was awarded the Society for International Nutrition Research's Kellogg Prize for International Nutrition.



EGYPT

GDP per capita:

\$4,200

Percentage of adults
who are overweight or obese:

59.1 (1998)

In Egypt the obesity problem is particularly severe for urban women. Poor Egyptians have adopted modern habits that exacerbate obesity, such as television watching.



rie unit on a food packaging label, though, is equal to 1,000 heat-energy calories, so it is often called a kilocalorie, or kcal for short. Daily energy requirements vary depending on age, weight and activity levels, but most nutritionists recommend a range of 1,800 to 2,200 kcal for women and 2,000 to 2,500 kcal for men. When a person consumes a surplus of 3,500 kcal above his or her requirements, this extra amount will usually produce a weight gain of about 0.45 kilogram (one pound). Researchers estimate that putting sweeteners into beverages added about 137 kcal to the average American's daily diet between 1977 and 2006. Over a year this surplus can cause a weight gain of about 6.4 kilograms (14.2 pounds). In Third World countries, consumption of sweeteners is rapidly catching up to American levels; for example, the average Mexican now consumes more than 350 kcal from beverages every day.

The growing presence of supermarkets in the developing world has greatly increased the availability of both sweetened beverages and processed foods. In country after country, companies such as Wal-Mart, Carrefour and Ahold have opened giant stores offering a wide variety of cheap snacks and soft drinks. In Latin America the proportion of all food expenditures spent in supermarkets jumped from 15 percent in 1990 to 60 percent in 2000 and is still rising briskly. Scientists have not yet quantified the impact of replacing traditional village markets with megastores, but the few studies available suggest that the new way of shopping encourages the consumption of processed

foods, particularly products with added sugar.

Another key contributor to obesity is the widespread shift to energy-dense foods that has occurred in many developing nations. The human body regulates appetite based on the volume of food consumed rather than the number of calories in a meal. This adaptation was useful in regions where large seasonal swings in rainfall and temperature affected food production; during the times of plenty, people could load up on calorie-rich meats and vegetable oils, building up their weight to survive subsequent periods of famine. In recent years, however, the consumption of energy-dense vegetable oils—soybean oil, palm oil, corn oil and dozens of variations—has skyrocketed in the developing world. In China, for example, the average daily intake of vegetable oils rose from 14.8 grams per person in 1989 to 35.1 grams per person in 2004, adding an extra 183 kcal to the population's daily diet. Similar increases have taken place in the Middle East, Africa, and parts of South and Southeast Asia. My research has shown that technological advances in the production and processing of oilseeds have made vegetable oil a relatively cheap option for poor families; in China, the poor spend a larger share of their food expenditures on vegetable oil than the rich do.

The third major change in the developing world's diet is the surge in consumption of animal-source foods. Over the past 20 years most of the growth in the world's production of meat, poultry, fish, eggs and milk has come from developing nations. Latin Americans are eating more beef, Chinese are devouring more pork and

REUTERS (photograph)

Indians are consuming more dairy products. In China the consumption of animal-source foods more than tripled in rural areas and almost quadrupled in urban areas between 1989 and 1997. By 2020 developing countries are expected to produce nearly two thirds of the world's meat and half its milk. In addition to raising obesity rates, the intake of all this energy-dense animal-source food threatens to boost the prevalence of heart disease in the Third World by injecting excessive saturated fat into the average diet.

People in the developing world are not only converting to the unhealthy Western diet; they are starting to work, travel and entertain themselves in ways that worsen that diet's effects. When I lived in Asia in the 1970s, only small quantities of electricity reached rural areas, roads were unpaved and farming was the only option for employment. What is more, farming in Asian countries was a backbreaking task: transplanting rice, weeding, hoeing, spreading fertilizer and harvesting were all done by hand. Difficult manual labor was also the norm for people living in the urban slums of Old Delhi in India, where I lived for a year.

Today, however, the various components of modern infrastructure—roads, factories, media access, and so on—are reaching into even the remotest corners of the Third World. Many farmers in Asia and Latin America now use tractors

to plow the soil and trucks to carry their produce to market. In China the portion of the population working in jobs with very light activity requirements has grown from 44 percent in 1989 to 66 percent in 2004. In 1989 few Chinese owned a television; today televisions are ubiquitous in the country, with more than half of households owning a color set. Because the shift to a more sedentary lifestyle decreases one's energy requirements, excess calories accumulate faster. In our studies in China, my colleagues and I have shown that all the observed lifestyle changes—increased television use, reduced walking and biking, and less strenuous labor at home and in the workplace—have led to significant gains in weight.

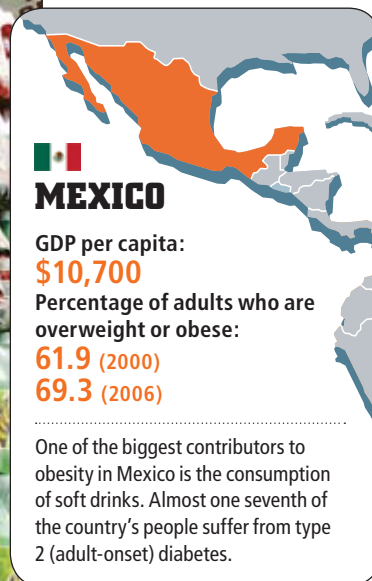
The Big Picture

The overarching trend that is encouraging all these changes in diet and lifestyle is globalization—the freer movement of capital, technology, goods and services across the world. For example, the ability of huge retailers to open mega-stores in developing countries has brought all the health effects of modern food processing, both positive and negative, to new populations. Global media companies have enhanced the attraction of television by offering entertaining programs to regions that formerly received only boring government-produced broadcasts. Fur-

The shift from undernutrition to overnutrition has occurred in less than a generation.



EDUARDO VERDUGO AP Photo (photograph)



It may be difficult to gather support for a fight against obesity, which is still widely viewed as a sign of sloth and gluttony.



CHINA

GDP per capita:
\$7,700

Percentage of adults who are
overweight or obese:

12.9 (1991) 27.3 (2004)

The booming Chinese economy has increased average incomes, enabling the country's people to boost their intake of calorie-rich foods while shifting to a more sedentary lifestyle.

thermore, international agencies such as the World Bank have promoted agricultural changes that have encouraged the proliferation of unhealthy diets in the developing world.

The long-held philosophy of agricultural experts is that once a country produces enough grains and tubers, it should massively subsidize its livestock, poultry and fish industries. The result has been a major reduction in the prices of animal-source foods. The wholesale price of beef (in real dollars) on the world market declined from about \$530 per 100 kilograms in the early 1970s to about \$150 per 100 kilograms in the mid-1990s. The drop in the cost of vegetable oils and animal-source foods, combined with the recent increases in personal incomes in China, India and other developing nations, has led to a consumer revolution. People are rapidly abandoning their traditional low-fat, high-fiber diets and switching to meals of calorie-rich fats, sweeteners and refined carbohydrates.

What can we do to counter such a sweeping and deadly transition? No country in modern times has succeeded in reducing the number of its citizens who are overweight or obese. In fact, the obesity epidemic is accelerating in the U.S. and many other nations. The world is getting fatter, and the annual rates of increase are higher today than they were 15 years ago.

Representatives of the food industry have long insisted that governments should not re-

strict an individual's dietary choices. Their solution is to teach people how to control their diets and become more physically active. Even most health professionals in the U.S. and abroad focus on the narrow, short-term need to educate children and their parents. But this strategy ignores the vast social, technological and structural changes that are pushing millions of people into debilitating lives of obesity. If left unchecked, the nutrition transition will cause horrendous increases in illness and devastating reductions in life expectancy.

In the developing world, most government and private aid programs still focus on fighting hunger and infectious diseases. These efforts can backfire, though; national hunger programs in Mexico and Chile may have increased obesity levels among some recipients of their food aid. For example, the Mexican program called Oportunidades (formerly named PROGRESA) has improved the growth rates of children in the families it has enrolled but has also exacerbated obesity among the urban women receiving its cash payments and food supplements. In response, the managers of the program are now considering halting the distribution of fortified milk to adult women and providing vitamin supplements instead.

It may be difficult for politicians or development officials to gather support for a fight against obesity, which is still widely viewed as



EUGENE HOSHIKO AP Photo (left); XIE HUANCHI AP Photo/Xinhua (right)

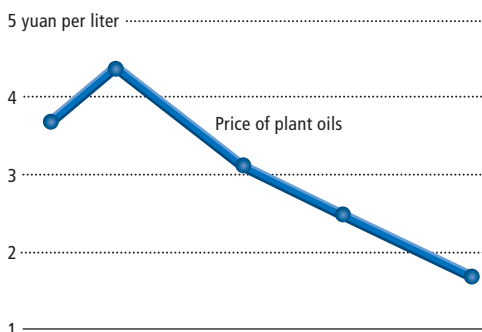
a sign of sloth and gluttony rather than as a consequence of global changes. Nevertheless, this new threat demands action. Nongovernmental organizations such as the Bill & Melinda Gates Foundation, which strives to improve public health and reduce poverty around the world, must address the obesity epidemic before it is too late. Unless strong preventive policies are undertaken, the medical costs of illnesses caused by obesity could bring down the economies of China, India and many other developing countries. China already spends more than 6 percent of its gross domestic product on nutrition-related chronic diseases, and this expense is projected to increase steeply over the next 20 years.

Government interventions will also be necessary. We could begin by restructuring the massive agricultural subsidies that encourage the production of meat, poultry and dairy products. Instead of giving billions of dollars to giant agribusinesses growing grain for livestock, the U.S. and other high-income nations could direct some of that money to farmers cultivating fruits and vegetables. This reform could help people in developing countries by adjusting prices on the world market. Making meat more expensive and vegetables cheaper would provide an incentive for healthier food choices. New farm policies should also promote the global consumption of whole grains, which have more fiber, vitamins and minerals than refined carbohydrates.

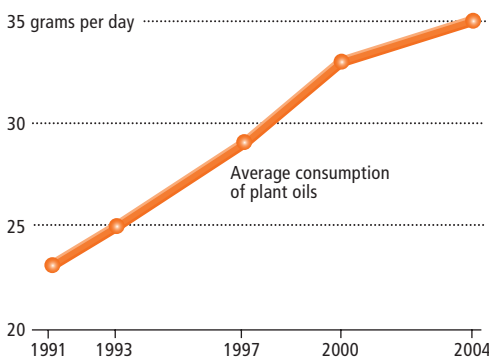
Revamping subsidies will not be as effective for discouraging the consumption of sweetened foods and beverages, because the cost of sweeteners represents just a small fraction of the price of such products. An alternative might be to tax all caloric sweeteners (including sugar, high-fructose corn syrup and concentrated fruit juice) at a relatively high rate—say, a nickel per gram. In Mexico, which has one of the highest consumption rates of soft drinks in the Third World, I am working with the Ministry of Health to devise taxes on these and other high-calorie beverages. I am also working with the Chinese government on testing a tax on vegetable oil in selected provinces. We have found that taxing dietary fat can cut the total calorie intake while increasing protein consumption among the poor in China because they substitute healthier foods for the fats. The impact would be even more positive if the revenues from the tax were spent on encouraging better nutrition.

Researchers and development experts have

AS THE PRICE OF VEGETABLE OILS HAS DROPPED IN CHINA ...



... THE COUNTRY'S CONSUMPTION OF THESE CALORIE-RICH FOODS HAS CLIMBED.



proposed dozens of similar policies, but they must be designed to meet the specific needs of each country. One particularly intriguing proposal is to ban advertisements for sweetened foods and beverages from children's television or perhaps from all media. At the same time, we cannot forget that many people in developing nations still suffer from hunger. We must design aid programs that can meet the needs of the hungry without increasing obesity in those countries. Conversely, we must ensure that policies designed to fight obesity—such as reducing the consumption of vegetable oils and animal-source foods—do not hurt the undernourished. Fortunately, some options for fighting overnutrition will be just as helpful for combating undernutrition. For example, the promotion of breastfeeding and the increased intake of fruits and vegetables would alleviate both conditions.

Stemming the tide of obesity in the Third World is a tall order. More policy research is needed to determine the best ways to influence dietary choices in developing countries. Ever since our species arose, we have strived for a tastier diet and a more sedentary way of life. Now we need to reverse those tendencies if we are to create a healthier world.

FALLING PRICES for vegetable oils have fostered unhealthy diets in the Third World. In China, a steep drop in the prices of rapeseed, soybean and peanut oils has allowed even the poorest people to increase their intake of these calorie-rich foods.

MORE TO EXPLORE

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More information about the Nutrition Transition research program is available at www.nutrans.org

STILL HUNGRY

One eighth of the world's people do not have enough to eat

By Per Pinstrup-Andersen and Fuzhi Cheng

KEY CONCEPTS

- The world produces enough food to meet the energy and protein needs of every living person. Why, then, are so many people still hungry?
- Poverty renders millions of people unable to buy or grow adequate food.
- Policies to alleviate hunger must focus on eliminating poverty—most crucially on agricultural development, basic education and health services, and good governance.

—The Editors

During the 30 minutes it will take you to read this article, 360 preschool children will die of hunger and malnutrition. Twelve a minute, around the clock; more than six million a year. But that is only the tip of the proverbial and ugly iceberg. One in four preschoolers in developing countries suffers from hunger and nutritional deficiencies. These children do not grow to their full potential, they have little resistance to disease, they learn less in school and they earn less as adults. Because of low birth weight, they are handicapped from the moment they enter the world.

More than 800 million people—two and a half times the population of the U.S.—live every day with hunger, or “food insecurity,” as it is often called, as their constant companion. Many more have micronutrient deficiencies: they do not get essential vitamins or minerals in their diets. Insufficient iron, and the anemia that comes with it, is the most widespread of these maladies.

The problem does not stem, as some might

think, from insufficient production. The world is awash in food, and more and more people are overeating. The so-called nutrition transition, in which diets change from basic grains and tubers to meat, dairy products and processed foods high in sugar and fat, is in full force in developing countries, bringing with it a dual nutritional problem of deficiencies and hunger in some households and obesity and related diseases in others. Technological advances in agriculture mean more food is grown at lower cost than ever before. Globalization, improved communication and efficient transport have facilitated the movement of food over long distances at reasonable rates. In fact, enough food is now being produced to meet the energy and protein needs of every person on the planet. Knowledge about nutrition is widely available, and the large humanitarian and economic costs of hunger and malnutrition are well documented—as are the benefits of eliminating these afflictions.

The main reason hunger and nutritional deficiencies persist is poverty; many millions of



households simply cannot afford to buy nutritious food or the farming supplies they need to grow enough of their own. And this poverty is sustained by poor access to family planning and reproductive health care and by diseases that spread because of poor sanitation and dirty drinking water, among other factors.

Effective action to reduce hunger must be based on a thorough understanding of who the hungry are, where they are, and exactly why they are malnourished. In the pages that follow, we lay out the best current knowledge on these questions and on the steps that need to be taken to feed the world.

Who Are the Hungry?

Hunger may be long-term, or it may be transitory. Long-term hunger is pervasive among people caught in the trap of poverty. Although not all poor people are hungry, almost all hungry people are poor. The great majority—75 percent—of the chronically underfed live in rural areas of developing countries. They are landless,

frequently unemployed or employed at very low wages. Or they are farmers with small land holdings and limited access to other assets, credit and agricultural necessities such as fertilizers and crop protection. They live in households headed by women with little wage-earning capacity or in households in which the adults suffer from illnesses such as HIV/AIDS. They are orphans and other individuals without families. They are usually invisible to decision makers in the societies where they reside, and the term “silent hunger” describes their condition poignantly.

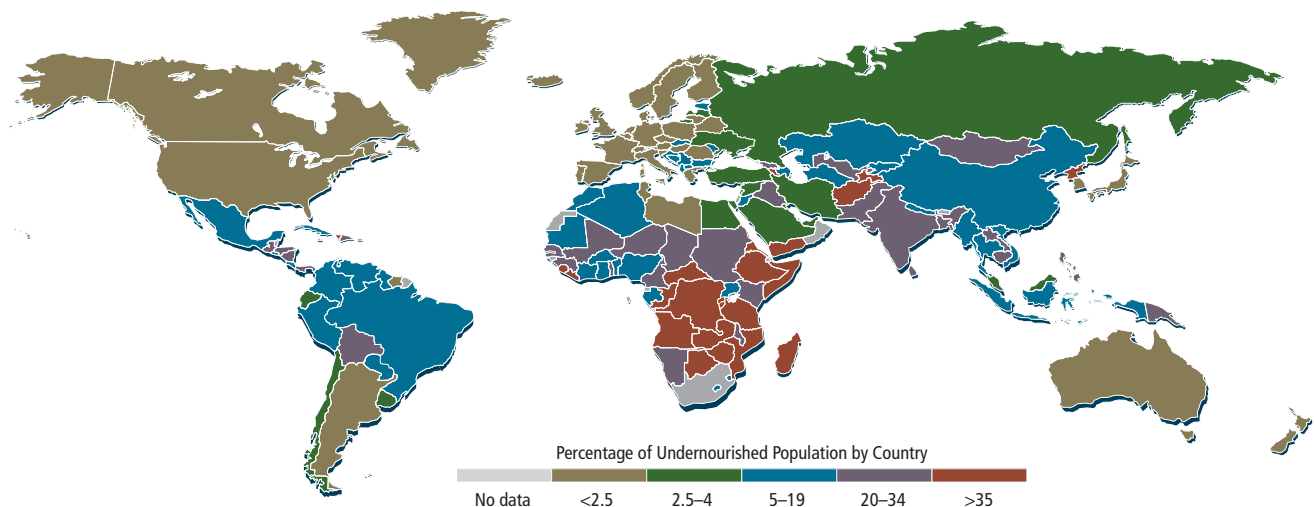
Transitory hunger caused by natural or human-made disasters such as droughts, floods, earthquakes, conflicts or bad policies tends not to be silent. Most of us have seen haunting images of the starvation that occurs during such famines. And the world has demonstrated its generosity in helping the victims of transitory hunger, although they represent only a small part—roughly 10 percent—of the world’s hungry. Like the chronically hungry, they are usually found in ru-

▲ **FAMINE VICTIMS in Ethiopia in 2006 present a stark reminder that malnutrition is far from conquered.**

HUNGER HOT SPOTS

The great majority of the world's underfed live in rural areas of developing countries. The highest percentage (see map below) are in Africa, although the Asia-Pacific region has the largest absolute number

of poor and food-insecure people. Drought is the leading cause of hunger worldwide; in recent years, however, armed conflicts are precipitating an increasing number of food crises.



Hunger, unbalanced energy intake and vitamin and mineral deficiency account for more than half the world's disease burden.

—Food and Agriculture Organization (FAO) of the United Nations

ral areas, primarily in Africa and Asia. These rural populations depend almost exclusively on agriculture; they have very few alternative sources of income, and they are therefore very vulnerable to shocks of nature. Although natural disasters continue to undermine people's food security in various regions of the world, hunger hot spots in recent years have switched to areas affected by human-induced devastation. Between 1992 and 2003, armed conflicts and economic problems accounted for more than 35 percent of food emergencies, compared with around 15 percent between 1986 and 1991.

Hunger and malnutrition affect two groups of people disproportionately. The first is preschool children: some 146 million are underweight because of chronic or acute hunger. This means that 18 percent of all hungry people are children younger than five years. Child hunger is frequently passed on from mothers who themselves are malnourished; about 20 million children are born underweight annually. Undernourished youngsters are less motivated to play and study, and many fail to get even the most rudimentary education. Millions leave school prematurely. Chronic hunger also delays or stops physical and mental growth. Most tragically, infectious diseases such as measles or whooping cough can kill undernourished children more readily than well-fed ones.

Women and girls are also more likely to be victims of hunger: more than 60 percent of the world's hungry are female. Although women are by and large the main producers of food throughout the world, social structures and traditions often mean that they get less to eat than men do. For example, whereas around 25 percent of men in developing countries have anemia caused by a lack of iron, 45 percent of women in the same regions are affected. Every day 300 women die during childbirth because of iron deficiency.

Where Are They?

The Food and Agriculture Organization (FAO) of the United Nations estimates that an annual average of 854 million people were undernourished over the period from 2001 through 2003: 820 million in developing countries, 25 million in transition countries (such as the former members of the Soviet Union) and nine million in industrial countries. A disproportionate share of the poorest and most food-insecure people live in Africa, although the Asia-Pacific region has the largest absolute number of chronically undernourished residents. The developing countries as a group did see declines between the periods of 1990–1992 and 2001–2003, but the numbers rose by eight million in South Asia (which includes India) and by 37 million in sub-Saharan Africa.

Recent statistics show that in developing countries, 27 percent of children younger than five are underweight and 31 percent are stunted. In several large South Asian countries (India and Bangladesh among them), both underweight and stunting rates are well above those in the region as a whole and much higher than those in Africa. Undernutrition in children is the worst in Asia in terms of absolute numbers, but because the Asian region is doing well at an aggregate level, chances are that these high undernutrition rates will escape the attention of governments and relief organizations unless special efforts are made to highlight this issue.

Why Are They Hungry?

Hunger can have many causes. As noted, insufficient food production on the global scale is not one of them. The world as a whole produces more than enough food to feed all the hungry; it is the unequal distribution of food among and within countries that has led to the world hunger problem.

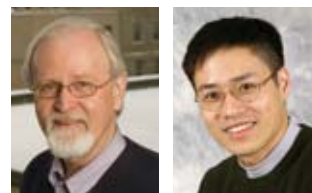
Unequal distribution has its deep root in poverty: in times of food shortages, the poor country simply cannot buy enough food in the world markets, and even when food is available inside the country, the poorest of its citizens are often unable to pay for it. Poverty also limits the production of food in impoverished areas, because the destitute lack the resources to invest in agriculture.

The natural disasters such as floods, storms and drought that are the primary causes of transitory or acute hunger have increased over the past decade, and the consequences for poor countries have been severe. Drought is now the leading cause of famine throughout the world. Episodes of drought in 2004 led to heavy losses of livestock and crops in parts of Kenya, Uganda, Somalia, Eritrea and Ethiopia. In many countries, deforestation, salinization, and poor farming practices such as overcropping and overgrazing are exacerbating the natural disasters.

Food crises that can be attributed to human-induced causes have also increased in recent years. Armed conflicts in Asia, Africa and Latin America uproot millions of people and precipitate some of the world's most serious hunger emergencies. Escalating conflict in the Darfur region of Sudan in 2004 drove a million people from their homes and led to a major food crisis, despite the fact that the area had enjoyed relatively good growing conditions. In the 1990s, as fighting swept through Central Africa, the prevalence of hungry people rose from 36 to 56 percent, whereas the termination of armed conflict in Mozambique brought rapid economic growth and reduced poverty. More peaceful parts of Africa, such as Ghana, have seen decreasing levels of malnutrition.

HIV/AIDS exacerbates the plague of hunger. At the household level, the disease has caused food insecurity by leaving millions of children

[THE AUTHORS]



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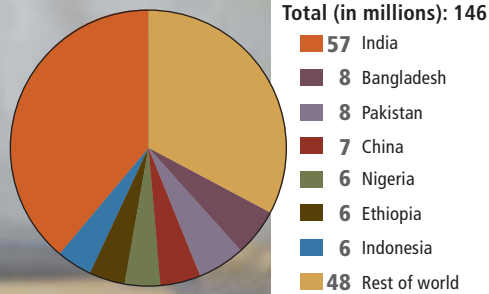
▲ **FOOD PRODUCTION** is limited in many places, such as this farm in India, because the destitute lack resources to invest in agriculture. Hunger then becomes chronic.



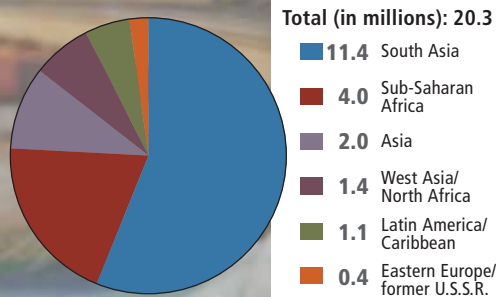
▲ **HUMAN-INDUCED DEVASTATION**, such as the conditions in North Korea, where these people line up outside a food distribution center, causes more transitory malnourishment.



WHERE ARE THE UNDERWEIGHT CHILDREN?



WHERE ARE THE LOW-BIRTH-WEIGHT BABIES BORN?



▲ **WOMEN AND CHILDREN** account for the majority of the hungry: roughly 500 million women are malnourished; 146 million pre-school children are underweight (*top chart*). Child hunger is often passed on from mothers who themselves are malnourished and give birth to underweight infants (*bottom chart*).

without providers, depleting assets, increasing medical expenses, and diverting resources from sustainable investments. At the national level, it has reduced the ability of countries to prevent and mitigate food emergencies by taking the lives of crucial producers and professionals in different sectors of the economy. The negative effects of the pandemic are reinforced by other crises—poverty, fighting, misuse of resources, and climate stress, which together create a vicious cycle of malnutrition and disease.

What Can Be Done?

The nations of the world have not ignored hunger, but despite nice rhetoric and promises, their efforts have fallen short. At the 1996 World Food Summit political leaders from virtually every country agreed to reduce the number of hungry people by half, from roughly 800 million to about 400 million, over the 25-year period from 1990 to 2015. The same countries met five years later to take stock of progress. Although some, such as China, had made strides toward achieving the target, over half the countries, mainly in sub-Saharan Africa, had *more*

hungry people, and at the global level the total number had not changed significantly. The leaders renewed their promise to halve the number of hungry people, but developments since then indicate that they have taken very little new action.

A different group, the Millennium Summit, reaffirmed the target in 2000, albeit as the easier goal of halving the *proportion*, rather than the absolute number, of people who are hungry. Although East and Southeast Asia and Latin America are likely to reach this goal, it will

not be attained globally. Between 800 million and 900 million of the world's citizens will still be hungry in 2015.

Implementing rapid economic growth for poor people is the backbone of any strategy to eliminate hunger and malnutrition. The specific policies that will be most fruitful will vary according to local and national circumstances. But, as we will demonstrate below, they definitely include programs supporting rural development, with an emphasis on agriculture, as well as basic education and health services, and good governance.

Because 75 percent of the world's poor live in rural areas, the most crucial component may well be agricultural and rural development. According to the FAO, in all the countries on track to reach the Millennium Development Goal, increases in income in the agricultural sector are significantly better than average. Yet many developing countries ignore this observation and continue to give priority to urban development. The bias against agriculture deters investment in infrastructure such as roads, warehouses and irrigation that would benefit farmers.

The promise of agricultural development was demonstrated many years ago in South Korea, Taiwan, India and several other Asian countries during the so-called green revolution. In the 1960s and 1970s innovations put in place by the Consultative Group on International Agricultural Research and collaborating national

institutions culminated in dramatic increases in rice and wheat yields, decreased costs of production, lower food prices, higher incomes for small farmers and, ultimately, avoidance of an impending hunger catastrophe.

Among the policies directed at agriculture that are needed to pull the farmers of developing countries out of poverty are ones ensuring secure access to land and to technologies such as fertilizers, improved seed and better protection of plants against pests. Investments in rural infrastructure—roads, electrification, storage facilities and irrigation—are also essential. So are the availability of credit and savings institutions. Because well-functioning markets for selling produce and buying consumer goods will be crucial, governments must ensure that markets are not biased against small farmers, less favored areas (those with irregular rainfall and fragile soils, for example) and poor consumers. Brazil's efforts under President Luiz Inácio Lula da Silva to give land to poor rural people is an illustration of a successful, albeit limited program. In China, promotion of small-scale rural enterprises providing goods and services for farm families, as well as rural-based agro-industries (such as food processing), which create employment and add value to agricultural produce, have played a major role in reducing poverty and hunger.

Many antipoverty policies—particularly

those promoting health and education—will benefit both the urban as well as the rural poor, which is important because urban destitution is on the rise. Past experience indicates that the most successful measures focus on fighting widespread micronutrient deficiencies, reducing food contamination and food-borne illnesses, and providing universal primary education for girls and boys. Policies and behavioral changes that encourage gender equality in decision making and in sharing resources are extremely valuable because women are a critical link in the well-being of households. Family-planning counseling and reproductive health care in forms compatible with local cultures are also key pieces of the solution. Examples of successful programs include PROGRESA, which has improved access to education, health care, clean water, safe sanitation and child care in Mexico, and the Food for Education Program, which has increased school attendance and reduced hunger among children in Bangladesh [see boxes on next two pages].

Technological developments in the biological sciences, energy and communications offer new opportunities that could benefit poor people and thus ease hunger. For instance, in China and India, government approval of the genetically modified cottonseed Bt cotton, whose plants are resistant to the attack of certain insects such as the cotton bollworm, has resulted

THE PERILS OF CHILDHOOD MALNUTRITION

Malnutrition plays a role in more than half the annual 12 million deaths of children younger than five.

Every year up to 500,000 children become partially or totally blind because of vitamin A deficiency.

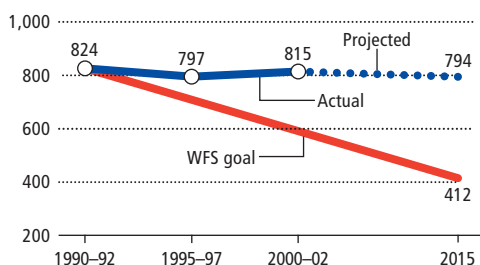
Iodine deficiency is the single most important cause of preventable brain damage in children.

—FAO

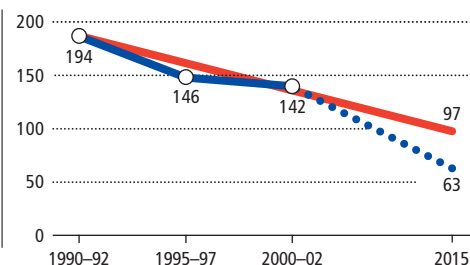
PROGRESS TOWARD MEETING THE WORLD FOOD SUMMIT GOAL

GLOBAL

Undernourished people (millions)



CHINA



The 1996 World Food Summit pledged to reduce the number of hungry people by half by 2015. As that year approaches, however, the total number remains little changed (*left graph*). China, in contrast, although it is still a developing nation, has made huge progress (*right graph*), becoming the world's third largest food aid donor in 2005. In the photo, a Chinese worker prepares relief goods bound for victims of an earthquake in Pakistan.

FIGHTING HUNGER ON SEVERAL FRONTS

Once oppressed by famine and dependent on food imports, Bangladesh now not only produces almost all its own rice but also exports agricultural products, and its gross domestic product is growing. As Gordon West, formerly of the United States Agency for International Development, has pointed out, this turnaround resulted from several smart interventions.

The ability to grow rice during the dry season drove much of this transition. At one time, most rice production in the nation depended on monsoon rains. Then public research institutions developed and released rice varieties that grow abundantly in cooler weather and that require fewer daily hours of sunlight. By 2002, about half of the country's rice crop was being produced in the dry months.

Another important prod to change was government institution of a more flexible import policy. As a result, private traders began bringing food in at times when the nation did not produce enough for itself. The government also gave more attention to targeting food distribution to the impoverished. For example, a food-for-education program was begun that gives food to poor families when their children attend school instead of working. In addition to improving

nutrition, this program has allowed youngsters to reach higher levels in school.

Foreign development agencies helped as well: they financed the construction and repair of roads, creating jobs and improving year-round access not only to markets but to basic services. Other agencies—notably CARE and World Vision—gave jobs to men and women in the most food-insecure areas of the country. In addition to building environmentally sound, all-season roads, participants plant trees to prevent soil erosion, and poor women find further employment in caring for the trees. In a similar vein, the United Nation's World Food Program paid people with food when they worked to restore important community resources such as roads, ponds supporting fish, and embankments that provided protection from floods.

Although the changes that occurred in Bangladesh are impressive, huge challenges remain. Rates of malnutrition continue to be among the highest in the world. Because the diets of many Bangladeshis are deficient in essential fats, minerals and vitamins, an important next step for the country will be making products such as wheat, fruit, milk, legumes and meat more widely available. —*The Editors*

VEGETABLES at a local market—adding meat and milk to the selection would boost nutrition. The children in the photo on the right exercise at a school that participates in the food-for-education program.



in major economic gains for millions of small farmers. Public investment in research and technology is needed to develop other innovations, and farmers and consumers should participate in setting priorities for this research.

Good governance, including the rule of law, transparency, absence of corruption, conflict prevention and resolution, sound public administration, and respect and protection for human rights, is of critical importance to assure sustainable food security. Zimbabwe, which over a short period moved from being a food-secure country to one with widespread hunger, demonstrates what can happen in the absence of

good governance. Although national governments bear the primary responsibility, civil society, as represented by local community-based groups and NGOs (nongovernmental organizations), can also assist low-income people.

Internationally, policies and institutions need to do more to guide globalization for the benefit of the poor. Industrial countries should accelerate opening their markets, and the World Trade Organization should work closely with civil society and national governments to remove barriers that hinder the movement of laborers across borders, distort prices, impose unfair intellectual-property rights, and choke

PAYING PEOPLE TO ATTEND SCHOOLS AND CLINICS

Two decades ago rising poverty in Mexico meant that almost one out of three people did not have enough to eat. Poor nutrition leads to bad health, which slows down learning capacity, which breeds poverty, which leads back to poor nutrition. So, in an example of a program that has worked well, the government introduced an innovative plan. Instead of subsidizing tortillas—which it had been doing and which provided only temporary relief from hunger—the government began paying women directly if they took certain actions.

Called PROGRESA (renamed Oportunidades), the program gives monthly cash payments—of up to about U.S. \$61—for each child in grades three through nine who attends school, and awards higher amounts for those in higher grades and for girls. Each family also receives monthly food transfers worth roughly \$14 if family members, especially mothers and children, make a specified number of clinic visits annually.

Perhaps the most unusual feature of the program is its channeling of funds to women. This economic power could give women a larger voice in decision making within households, which could potentially focus more of the family's resources on nutrition and education.

The plan's achievements already reflect improvements in both these areas. Participating families saw a 16 percent increase in the annual growth rate of children one to three years old and an almost 25 percent reduction in illness among children younger than five. Secondary school enrollment rose from 67 to 75 percent for girls and from 73 to 78 percent for boys, forecasting hope for even greater improvements as a better educated generation starts its own families. —*The Editors*



WOMAN RECEIVES MONEY provided by a program in Mexico that aids poor, rural families if they send their children to school and regular clinic checkups.



competition. The U.S., the European Union and Japan have erected trade barriers against imports of food and agricultural commodities produced by poor farmers in developing countries. At the same time, they pressure developing countries to open up their markets for the products of industrial nations, including highly subsidized agricultural commodities. These practices are worse than hypocritical; they actively hinder efforts to reduce hunger.

Development assistance should be increased from the current 0.3 percent of national incomes of donor countries to the 0.7 percent the rich countries have repeatedly pledged to give

since first adopting this commitment in a U.N. resolution in 1970. Ongoing negotiations for debt relief for low-income developing countries should be accelerated.

Winning the fight against hunger would not only benefit those who are hungry. We would all gain. Hungry people make poor trading partners, and they contribute to instability across nations. Even in a hypothetical world governed by purely selfish people who have plenty to eat, eradicating hunger would be a good idea. The world has the resources and the knowledge to win the fight. We have not yet shown that we have the will.

MORE TO EXPLORE

Consultative Group on International Agricultural Research, an alliance of agricultural centers and other organizations that mobilize science to help the poor: www.cgiar.org

Food and Agriculture Organization of the United Nations: www.fao.org

International Food Policy Research Institute: www.ifpri.org

SOWING A GENE REVOLUTION

A new green revolution based on genetically modified crops can help reduce poverty and hunger—but only if formidable institutional challenges are met

KEY CONCEPTS

- Genetically modified crops can increase the profits of farmers in developing nations and reduce food prices for poor consumers, but they are not a panacea.
- Unlike the green revolution of the 20th century, in which public research institutes developed technologies and freely disseminated them around the world, today's "gene revolution" is led by multinational corporations.
- Reaping the full potential of biotechnology in the developing world will depend as much on institutional factors (such as intellectual-property rights and environmental and food safety regulations) as on the development of transgenic crops suited to the local conditions in each country.

—The Editors

By Terri Raney and Prabhu Pingali

The number of hungry people in the world remains stubbornly high. In 1960 roughly one billion people were undernourished; tonight about 800 million still will go to bed hungry. Yet the progress in filling empty bellies has been much more substantial than those two numbers might suggest, because today around 5.6 billion people are fed adequately, compared with only two billion half a century ago.

Modern agricultural technology has been the key to these dramatic gains. The development and distribution of high-yield seeds and the inputs (fertilizers and irrigation) to make them grow to their full potential drove the green revolution of the 20th century. Conventional methods of selective breeding and the crossing of different varieties produced hybrids with desirable characteristics that increased farm productivity and incomes and brought down food prices.

Now we could be witnessing a nascent "gene revolution." In recent decades, researchers have developed and honed techniques to transplant individual genes from one organism to another, creating cultivars with valuable new traits. For example, a gene from the soil bacterium *Bacillus*

thuringiensis, transferred to cotton, maize and other plants, leads to so-called Bt varieties that have an innate resistance to insects such as borer beetles. In similar fashion, scientists have invented herbicide-tolerant soybeans, more nutritious, beta-carotene-enriched Golden Rice and some other superior crops.

Transgenic crops are spreading faster than any other agricultural technology in history, despite continuing controversy about potential risks such as gene flow (the escape of inserted transgenes into related crops or wild plants), the emergence of resistant pests, and fears that eating genetically modified foods might affect the health of consumers. The U.S. and Canada grow the bulk of transgenic crops—60 percent by area cultivated—but developing countries accounted for 38 percent in 2006, almost all of that in Argentina, Brazil, India and China.

If the promise of genetically modified crops to reduce hunger significantly is to reach full fruition, however, the crops must prove their economic value to poor farmers, who will grow them only if they can increase their profits by do-





ing so. Recent peer-reviewed studies have shown that farmers in developing countries have indeed benefited by growing transgenic crops. These farmers saw increased yields and lowered expenditures on pesticides that more than compensated for the higher costs of the transgenic seeds. In some cases, smaller farms gained proportionally more profit than larger farms did, contradicting the widely held perception that transgenic crops help only large farms, which can take advantage of economies of scale. The data also run contrary to the fear that multinational biotechnology firms are capturing all of the economic value created by transgenic crops. Rather consumers and farmers share the benefits with the firms.

The studies revealed, however, that profitability varied greatly from country to country or even between regions within a nation. At least as important as the performance of the

technology are institutional factors—the agricultural research capacity of a nation, the functioning of its agricultural input markets (such as distribution of seeds) and the overall policy circumstances, including regulations relating to the environment, food safety, trade and intellectual-property rights. Only if formidable institutional challenges are met can transgenic crops achieve their full potential to improve the livelihoods of farmers in the developing world.

In addition to increasing food production and reducing poverty, transgenic crops could alleviate some environmental problems caused by intensive agriculture. For instance, farmers who grow Bt crops can reduce their use of chemical pesticides that do harm to nontarget species such as bees. Herbicide-tolerant crops let them decrease their use of the most toxic compounds, albeit with an overall increase in lower-toxicity herbicides. Herbicide-tolerant crops are also as-

THE GENETICALLY MODIFIED WORLD

Twenty-two countries, both industrial (*blue*) and developing (*brown*), grow genetically modified crops. The map below presents a selection of facts about the development and commercial production of transgenic crops in developing nations; much more is under way.

MAJOR DEVELOPING-WORLD PLANTINGS OF TRANSGENIC CROPS

- **Soybean:** Argentina, Brazil, Paraguay
- **Maize:** Argentina, South Africa
- **Cotton:** China, India, Argentina, South Africa

IRAN

- Only country to approve Bt (insect-resistant) rice for commercial cultivation

CHINA

- On the brink of approving Bt rice for commercial cultivation
- Only developing country where farmers are cultivating transgenic crops (insect-resistant cotton) developed independently of the international private sector

THE PHILIPPINES

- Field trials of locally adapted Golden Rice to begin in late 2007

EASTERN AFRICA

- Maize streak virus is endemic

INDIA

- Indian researchers have developed transgenic eggplant, maize, pigeon pea, mustard, tomato, rice, okra, cabbage and cauliflower. Initial small-scale field trials are under way

BANGLADESH, CHINA, INDIA, INDONESIA, THE PHILIPPINES, SOUTH AFRICA, VIETNAM

- Research institutes are working with Syngenta to develop locally adapted varieties of Golden Rice

SOUTH AFRICA

- First developing country to plant a transgenic staple food (2001, Bt white maize)
- University researchers developed maize resistant to maize streak virus
- Preliminary work is under way on developing maize tolerant of drought based on genes from plants indigenous to Africa

AFRICA IN GENERAL

- Staple crops with no transgenic varieties yet available: sorghum, chickpea, cassava, pearl millet, pigeon pea and groundnut

ARGENTINA

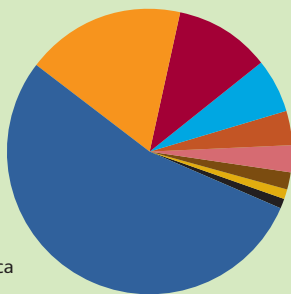
- Tremendous increase in soybean production credited to profitable transgenics

Most transgenic crop plantings are in the U.S. (*below left*), but since 2000, plantings have increased faster in developing nations than in industrial ones (*below middle*). A small number of crops and kinds of modification account for almost all the production (*right*).

THE BIG GROWERS

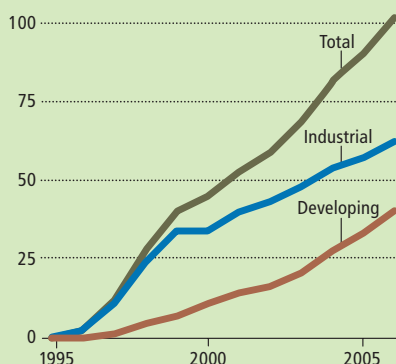
Transgenic crop area by country (2006)

- **54% U.S.**
- **18% Argentina**
- **11% Brazil**
- **6% Canada**
- **4% India**
- **3% China**
- **2% Paraguay**
- **1% South Africa**
- **1% Others**



RAPID INCREASES IN TRANSGENICS

Millions of hectares planted



KINDS OF PLANTINGS (2006)

Crops

- **57% Soybean**
- **25% Maize**
- **13% Cotton**
- **5% Canola**

Other biotech crops: rice, squash, papaya and alfalfa (less than 1%)

Traits

- **68% Herbicide tolerance**
- **19% Insect resistance**
- **13% Both**

sociated with the adoption of low- or no-till cropping practices, which reduce soil erosion and the disruption of soil structure and microbial communities. Thus, transgenic crops could help bring about a “doubly green revolution.”

Technology Is Vital

It is unfashionable to focus on agriculture and technology as a means to address poverty and hunger. Critics argue—correctly—that the world produces enough food to provide everyone with an adequate diet and that what is required is more equitable access for the poor. They extrapolate from these sensible observations to the mistaken conclusion that technological advances are unimportant or even counterproductive in the fight against poverty and hunger. The evidence proves them wrong. Technological innovation in agriculture is necessary (though not sufficient) to create sustainable economic growth and alleviate poverty in developing countries.

Agriculture is the fundamental driver of economic growth in agrarian societies. The technologies that fueled the green revolution brought enormous benefits to poor people. Modern varieties of wheat, rice and maize became available to millions of poor farmers in the developing world, first in Asia and Latin America and later (though to a lesser degree) in Africa. By raising agricultural productivity, the green revolution lifted farm incomes and reduced food prices, making food more affordable for the poor. This virtuous cycle of rising productivity, improving living standards and sustainable economic growth has lifted millions of people out of poverty.

The gene revolution, however, differs in significant ways that raise fundamental questions about whether poor farmers in developing countries will have access to appropriate transgenic crops on favorable terms. Multinational corporations conduct most biotech research—in contrast with the public-sector researchers at national and international levels who were behind the green revolution. And whereas those public institutions freely disseminated and shared the agricultural technologies of the last revolution, multinationals hold their inventions under exclusive patents and distribute them commercially. This shift in the source of the technology affects the kind of research that is being done, the type of products being created and their eventual accessibility for poor farmers.

China is the only developing country where farmers are cultivating transgenic crops developed independently of the international private

sector. Some developing countries—notably India, Brazil and South Africa—are conducting field trials on independently developed transgenic crops, but they have not been released for commercial production. Few others have the technical capacity for independent transgenic crop research and development. The Consultative Group on International Agricultural Research (CGIAR) system, a partnership of countries, organizations and private foundations, supports the work of some international research centers that are collaborating with national research systems and the private sector on transgenic crops for developing countries, but these programs are small and poorly funded.

Private-sector biotechnology research is naturally focused on highly profitable technologies suitable for farms in the temperate-zone environments of North America and Europe. Some farmers in developing countries (primarily in temperate zones in South America, South Africa and China) have taken advantage of “spillover” benefits from that work, but many others till in conditions, such as drought-prone regions of the tropics, that require dedicated solutions.

Very few major public- or private-sector programs are targeting crops and animals that the poor rely on or the particular problems that they face. Traits of special interest to the developing world include nutritional enhancement and resistance to production stresses such as drought, salinity, disease and pests. Crops that provide the majority of their food supply and livelihoods—rice and wheat—are being neglected, as are a variety of “orphan crops” (such as sorghum, pearl millet, pigeon pea, chickpea and groundnut). Those are staple foods in some regions and have also been largely passed over by conventional agricultural research programs.

Research for the Poor

Nevertheless, although their resources are dwarfed by those of programs aimed at more lucrative markets, researchers in many countries are working on transgenic approaches to the issues facing farmers in developing countries. Joel Cohen of the International Food Policy Research Institute surveyed the public research pipelines in 15 developing countries in 2003 and found 201 genetic transformations for 45 different crops, including cereals, vegetables,

[THE AUTHORS]



Terri Raney is senior economist in the Agricultural and Development Economics division of the United Nations Food and Agriculture Organization (FAO) in Rome and chief editor of *The State of Food and Agriculture*, the annual flagship publication of the FAO. Raney grew up on a small farm in Oklahoma and earned a Ph.D. in agricultural economics from Oklahoma State University. She lives with her husband on an olive farm in the Sabine Hills outside of Rome. **Prabhu Pingali** is director of the Agricultural and Development Economics division of the FAO. Originally from Hyderabad, India, he received a Ph.D. in economics from North Carolina State University and is an internationally recognized expert on the green revolution and technological change in agriculture. Earlier this year he was elected to the U.S. National Academy of Sciences as a foreign associate.

The views expressed in this article are those of the authors and do not necessarily reflect the views of the FAO.



For more about the green revolution, including discussion of criticisms about it, log on to: www.SciAm.com/ontheweb

roots and tubers, oil crops, sugar and cotton.

By far the most important food crop in the developing world is rice. Researchers are developing several transgenic rice varieties with farmers and consumers in poor countries in mind, including insect-resistant Bt rice and Golden Rice.

Field trials in China suggest that Bt rice can

help small farmers in many ways. By conferring resistance against some major crop pests, Bt rice reduces the need for chemical pesticides. Because farmers achieve better pest control, they gain higher effective yields at a lower cost. They also suffer less exposure to chemicals. (Small farmers in China typically use backpack sprayers with little or no protective gear and thus suffer high rates of insecticide poisoning.) The reduction in the use of broad-spectrum insecticides that kill many types of insects besides the target pests is also likely to be an environmental boon.

So far Iran is the only country that has approved Bt rice for commercial cultivation (on about 5,000 hectares in 2006). China is on the brink of permitting commercial cultivation of Bt rice but has held back, reportedly because of concerns about the possible loss of exports to nations that do not accept transgenic crops.

Golden Rice is perhaps the best-known transgenic crop developed specifically to meet the needs of undernourished people. It is designed to combat vitamin A deficiency, which claims 3,000 lives every day and causes half a million cases of infant blindness a year. For many of these people, up to 80 percent of daily calories consumed are from polished white rice, which contains no beta-carotene (the human body converts beta-carotene to vitamin A).

The first generation of Golden Rice included a gene from daffodils and another from a common soil bacterium, *Erwinia uredovora*, that together produce beta-carotene in the grain. Developed in 2000 by Ingo Potrykus of the Swiss Federal Institute of Technology in Zurich, Peter Beyer of the University of Freiburg in Germany, and a network of academic and humanitarian organizations, the original Golden Rice was sharply disparaged as a technological solution to a problem caused by poverty and social exclusion. Critics also argued that Golden Rice would encourage people to rely on a single food rather than diversifying their diets. They claimed that the money spent on developing Golden Rice would have been better devoted to enabling people to eat a balanced diet of grains, fruits, vegetables and proteins. Of course, many of the world's poorest cannot afford such meals, and these are the very people Golden Rice is intended to reach.

Detractors also noted that a normal serving of Golden Rice contained only a small fraction of the recommended daily allowance (RDA) of beta-carotene. Scientists at Syngenta therefore developed Golden Rice 2 by replacing the daf-

[GENES FOR AFRICA]

A CHAMPION FOR BIOTECH

Jennifer Thomson of the University of Cape Town in South Africa staunchly advocates transgenics for their potential to help alleviate hunger and poverty in Africa. In addition to leading a group developing varieties of transgenic maize crafted for African conditions, she has helped draft South Africa's regulations concerning genetically modified organisms and serves as chair of the Nairobi-based African Agricultural Technology Foundation (AATF).

Thomson's research group has spent 12 years creating maize resistant to the maize streak virus, which is endemic in eastern Africa. The scientists fashioned laboratory lines of resistant maize and conducted successful greenhouse trials. Laboratory lines are easier to genetically engineer than typical plants, but their other characteristics make them of no use for agriculture. Thomson's group has therefore licensed its virus-resistance technology to Pannar Seed International in KwaZulu-Natal, which is "doing the lion's share of the commercialization," she says. "They have transferred our resistance into commercially viable lines, and they are ecstatic. We are working on our application for field trials."

Thomson's group also seeks to produce a drought-tolerant maize using genes from the "resurrection plant," *Xerophyta viscosa*, which can recover from 95 percent dehydration. That research is at a very early

stage, and the scientists are still determining which genes to transfer. "We're testing [genes] singly and we're going to be testing them in combination. It's going to be a long-term project," Thomson says.

She says it is "absolutely" important for developing nations to conduct their own biotechnology research, including adapt-

ing technologies invented by multinationals. "Multinationals aren't interested in the crops we are interested in in Africa," she explains. "For instance, in West Africa we are interested in cowpeas. What multinational is interested in cowpeas? The AATF transfers intellectual property in biotech agriculture from multinationals to Africa. We've recently done a very successful [transfer] for insect-resistant cowpeas." Through the AATF, multinationals "are being incredibly helpful" in Africa, she says.

Yet for her own research, she has "resolutely refused money from multinationals, to keep [the technology] in

the public domain." For many years the maize streak virus project has been funded largely by the Claude Leon Foundation, "a philanthropic foundation that saw that virus-resistant maize would help Africans to survive." More recently Pannar has helped considerably, both financially and in kind (such as by testing the plants developed by Thomson's group). Says Thomson, "I don't want anybody to cause my maize to be more expensive." —**Graham P. Collins**



"RESURRECTION PLANT" can completely recover (top) from up to 95 percent dehydration (bottom).

fodil gene with an equivalent gene from maize. This modification increased the amount of beta-carotene by about 20-fold. Around 140 grams of the rice could provide a child's RDA for beta-carotene. In households that depend on rice for sustenance, a child's portion is typically about 60 grams, and he or she may eat several portions during the day.

Syngenta, a member of the Humanitarian Golden Rice Network, obtained free licenses from 32 companies and academic institutions for the humanitarian use of the patents needed to make Golden Rice. The company is working with public research institutions in Bangladesh, China, India, Indonesia, the Philippines, South Africa and Vietnam to develop locally adapted varieties of Golden Rice. Once the researchers have tested their varieties and obtained approval from the local authorities, the network will distribute them free of charge to farmers earning less than \$10,000 a year, and these farmers will be allowed to save and reuse seed from one crop to the next. In many prospective countries, however, locally adapted varieties cannot yet be developed and tested because the countries lack the proper biosafety procedures required by the international convention on biodiversity.

Challenges remain. Golden Rice must still be tested for environmental and food safety. In addition, human testing is necessary to determine how well the body absorbs the beta-carotene. The effects of storage and cooking must also be assessed. It is not clear how consumers will react to the color of Golden Rice, especially in cultures that prefer white rice. Field tests are scheduled to begin in Asia later this year. No one expects Golden Rice to be a magic bullet for malnutrition. But it could be a cost-effective supplement to other strategies.

Economic Evidence

The ultimate success or failure of transgenic crops will depend on whether farmers gain economic benefits from using them. Even when the private-sector research is well suited to conditions in a developing country, access to the technology may be expensive. The contrasting cases of insect-resistant Bt cotton and herbicide-tolerant soybeans in Argentina reveal how the high price of patented technology can stymie progress. Monsanto, which developed both types of cultivar, patented its cotton innovation in Argen-

KEY GM CROPS

Herbicide-tolerant soybeans fill the majority of genetically modified (GM) crop area in the world, including major plantings in South America.

Maize is a staple food in some developing countries and is also used as animal feed. It is sometimes grown in rotation with soybeans.

Rice is the primary staple food in much of the developing world, yet virtually no transgenic rice is under commercial cultivation.

Orphan crops—regional staple foods such as sorghum, pearl millet and pigeon pea—are being neglected by both biotechnology and conventional agricultural research programs.



tina but failed to do so with its soybeans. The company has thus been able to charge a significantly higher price for its Bt cottonseed than for conventional cottonseed. Consequently, the transgenic cotton offers relatively little benefit to Argentine farmers, who have not adopted it widely.

In contrast, Argentine farmers have enthusiastically embraced transgenic soybeans, for which less expensive seed (that Monsanto has not patented) is available. On average, productivity increased 10 percent on adopting farms, with the growers receiving nine tenths of the economic benefits. Globally, farmers receive only about 13 percent of the benefits of transgenic soybeans, with consumers taking 53 percent (through lower food prices) and seed and biotechnology firms 34 percent. Economists have credited the relatively cheap transgenics as the major factor in transforming soybean farming in Argentina, including a tremendous increase in the production of soybeans, the widespread adoption of no-till agriculture and the growing of soybeans in rotation with maize. No-till farming, in which farmers leave crop residues in place instead of tilling them into the earth, protects the soil from erosion and compaction and promotes the accumulation of organic matter. No-till farming is more practical with herbicide-tolerant crops, which allow farmers to control weeds with herbicides rather than tillage.

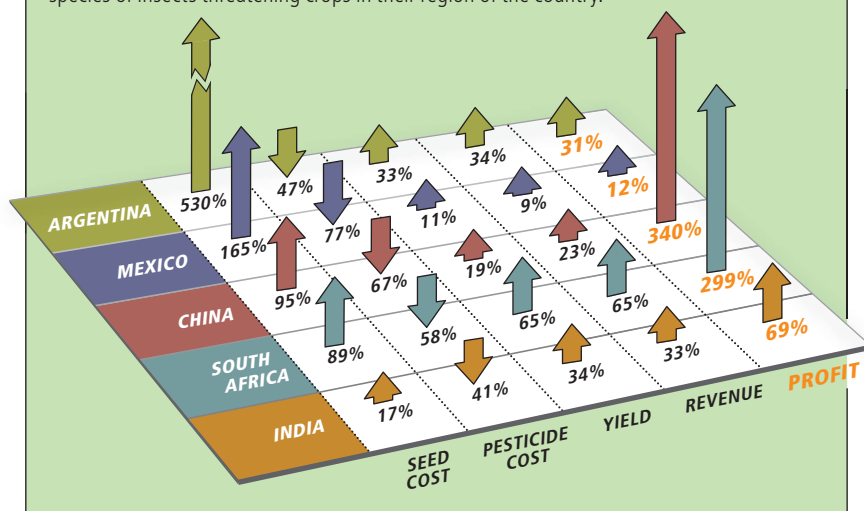
Yet the Argentine experience with soybeans does not present a model for solving the problem of access to biotech advances more generally. The protection of intellectual-property rights—through patents or other means—provides necessary incentives for technology developers and has greatly stimulated the growth of private agricultural research (albeit not necessarily in Argentina, as the private sector has simply brought into the country technologies developed in the U.S. and Europe). Existing public-sector international networks for sharing technologies across countries are being used less and less, however. The urgent need today is for a system of technology flows that preserves the incentives for private-sector innovation while at the same time meeting the needs of poor farmers in the developing world.

Otherwise countries must do as China has done. China has achieved success through its highly developed public agricultural research system, which has independently produced in-

[SOLID DATA]

THE TRANSGENIC ADVANTAGE

The experience of cotton farmers in five developing nations shows that even though the seed costs for a genetically modified crop can be much higher than for a conventional one, lower pesticide costs and higher yields and revenues can make the modified crops more profitable. The profits were very different, however, from country to country. In Argentina, seed costs took much of the substantial economic benefits away from the farmers. In China, competition from locally developed seeds kept seed prices relatively lower. Farmers there profited tremendously by slashing their heavy pesticide use. Mexico achieved only marginal yield gains. Also (not reflected in this chart) in many regions of Mexico few farmers adopted the transgenic cotton because of its poor effectiveness against the species of insects threatening crops in their region of the country.



sect-resistant crops by using a gene from cowpeas. Researchers have incorporated the gene into a large number of locally adapted cotton varieties that compete directly with Monsanto's Bt cotton. As a result, transgenic seed prices are much lower in China than elsewhere, and farmers reap substantially higher returns. In terms of productivity, farmer incomes, equity and sustainability, the 7.5 million small farmers who are growing insect-resistant cotton in China represent the most successful case so far of transgenic crop adoption in the developing world. The role of the public sector in developing and distributing the Chinese cotton varieties has been instrumental in achieving that success.

Chinese growers of transgenic cotton experience lower yield gains than in many other countries because pest damage on conventional cotton is controlled by heavy pesticide use in China. The farmers nonetheless achieve large net profit gains because their marginally higher yields are accompanied by much lower pesticide costs and only moderately higher seed costs. The significant reduction in pesticide use on cotton also has important benefits for the environment and for the farmers' health.

A 2003 analysis by Carl Pray of Rutgers University and Jikun Huang of the Center for Chinese Agricultural Policy concluded that the benefits of transgenic cotton in China were decidedly pro-poor: the smallest farms experienced the largest yield gains, and midsize farms had the largest reductions in total costs as a result of less pesticide use. In terms of net income, the percentage gains for small and midsize farms were more than twice those for the largest farms.

Our focus on cotton may seem odd in an article on reducing hunger, but it comes about because the most extensive peer-reviewed studies published to date on the outcomes of transgenic crop adoption in developing countries have been for insect-resistant cotton in Argentina, China, India, Mexico and South Africa [see box at left]. As far as foodstuffs go, such studies have been published only for soybeans and maize in Argentina and maize in South Africa.

The data for cotton crops are nonetheless highly relevant because they provide lessons in the economics of genetic modification that will be applicable to food crops. In addition, the cotton itself can improve the food security of many people: it can not only increase the cotton farmers' incomes but also raise the incomes of many other poor people in the wider economy when these farmers hire more laborers and buy more rural goods and services.

South Africa provides another important lesson about the role of institutions. That country has large, modern commercial farms operating alongside small-holder semisubsistence farms. Insect-resistant cotton and yellow maize (primarily used as animal feed) were introduced as long ago as 1998, and in 2001 South Africa became the first developing country to plant a genetically modified staple food (white maize).

For cotton, two studies of small-holder farmers in the Makhathini Flats of KwaZulu-Natal province in Africa have found that adopters of transgenics benefited economically. A local cooperative provided seed on credit, along with technical advice. The benefits were widely shared by all farm types, and both studies found significant pro-poor benefits. Pesticide use declined significantly, bringing both environmental and health benefits: cases of pesticide burns and sickness treated at local hospitals declined from about 150 cases in 1998–1999, when adoption was very limited, to about a dozen by 2001–2002, when adoption had become widespread.

The Makhathini Flats success story was not sustained, however. The local cooperative also

JEN CHRISTIANSEN; SOURCE: "ECONOMIC IMPACT OF TRANSGENIC CROPS IN DEVELOPING COUNTRIES," BY TERRI RANEY, IN *CURRENT OPINION IN BIOTECHNOLOGY*, VOL. 17, NO. 2, PAGES 174–176, APRIL 2006

POTENTIAL HAZARDS

Opposition to genetically modified crops or their products by consumers and advocacy groups, based on worries about food safety and harm to the environment, threatens to frustrate efforts to use biotechnology to alleviate poverty and hunger. The problem can be acute for developing countries, which often lack the capacity to formulate and implement their own regulatory procedures. International protocols do not permit transgenic organisms to enter a country or to be developed there if the country lacks appropriate regulatory procedures.

The chief food-safety concerns are fears that allergens or toxins may be present and that other unintentional changes in the food composition may occur. Yet to date no verifiable toxic or nutritionally deleterious effects resulting from the consumption of transgenic foods have been discovered anywhere in the world. National food-safety authorities of several countries have evaluated the transgenic crops currently being grown commercially and the foods derived from them, using procedures based on internationally agreed upon principles, and have judged them all safe to eat.

Environmental concerns center on the spread of transgenes to related crops or weeds ("gene flow"), the development of herbicide-resistant weeds, the development of insect pests resistant to the Bt toxin (which has long been used as a pesticide, particularly by organic farmers), harm by insect-resistant crops to nontarget organisms, and indirect environmental effects that come about because transgenic crops lead to different



ACTIVISTS in Mexico City protest the lack of information on labels of corn flour products containing genetically modified corn.

cropping practices.

Scientists disagree about the likelihood and potential consequences of these hazards. Gene flow, for example, is acknowledged to be possible when transgenic crops are grown close to related plants, but the transgenes will persist and spread only if they give the recipient plant a competitive advantage. Such gene

flow could inflict economic harm by, for instance, making a product ineligible for a status such as "organic." What would suffice to constitute ecological harm is more controversial.

Thus far, none of the major environmental hazards potentially associated with transgenic crops has developed in commercial fields. Herbicide-resistant weeds have been observed—although not necessarily caused by growing transgenic crops—and so far they can be managed by alternative herbicides. The lack of negative impacts so far does not mean they cannot occur, of course. Scientific understanding of ecological and food-safety processes is incomplete, but many of the risks highlighted for transgenics are similar to risks inherent in conventional agriculture as well. Careful, case-by-case evaluation of new crops (especially ones developed using new techniques, such as modification of multiple transgenes) must continue in order to minimize the potential for problems to emerge.

—T.R. and P.P.



For a longer discussion of the scientific consensus about the various safety and environmental concerns, log on to:

www.SciAm.com/ontheweb

OVERCOMING INSTITUTIONAL OBSTACLES

Developing countries need basic plant breeding capacity to adapt imported transgenic technologies into local crop varieties.

Countries need to adopt science-based, transparent and predictable regulatory procedures for testing the safety and efficacy of transgenic crops.

Companies and regulatory authorities should make public the results of their safety testing to minimize unnecessary duplication of tests done elsewhere.

Harmonization and mutual recognition of regulatory procedures at the regional and global level could help minimize unnecessary duplication and expense.

The protection of intellectual-property rights (IPRs) needs to balance the needs of technology developers and users (such as farmers). Possibilities include IPR clearinghouses and "open-source" sharing of technologies (such as www.bios.net).

➔ MORE TO EXPLORE

Agricultural Biotechnology: Meeting the Needs of the Poor? The State of Food and Agriculture 2003–04. FAO; 2004.

Poorer Nations Turn to Publicly Developed GM Crops. Joel Cohen in *Nature Biotechnology*, Vol. 23, No. 1, pages 27–33; January 2005.

From the Green Revolution to the Gene Revolution: How Will the Poor Fare? Prabhu Pingali and Terri Raney. ESA Working Paper No. 05-09. FAO; November 2005.

Economic Impact of Transgenic Crops in Developing Countries. Terri Raney in *Current Opinion in Biotechnology*, Vol. 17, No. 2, pages 174–178; April 2006.

ran the only cotton gin in the area, thereby ensuring a high rate of debt recovery. When another cotton gin opened in the region, the cooperative was no longer guaranteed repayment of its debts and ceased providing the transgenic seed on credit in 2002–2003. Cotton production in the region fell drastically. Researchers concluded that Bt plants could be an excellent technology for African countries but warned that institutional failure like that in the Makhathini Flats is the norm rather than the exception in Africa.

The Makhathini Flats example has relevance not just for Africa. No technology can overcome the gaps in infrastructure, regulation,

markets, seed distribution systems and extension services that hamper growth in agricultural productivity, especially for poor farmers in remote areas. Transgenic crops ought to be seen as one tool within a broader agricultural development strategy.

The ability of scientists to devise safe, effective transgenic crops for a gene revolution seems assured. What remains in doubt for a hungry person in a developing country is how long it will be before someone develops seeds suitable for farms in his or her province and those seeds become available on sufficiently attractive terms for local farmers to adopt them. ■

IS YOUR FOOD CONTAMINATED?

New approaches are needed to protect the food supply

KEY CONCEPTS

- Terrorist plots, greater imports and more centralized food production are raising the chances that food will be tainted by natural or man-made contaminants.
- Safety procedures adapted from military operations can tighten the physical security of food production facilities.
- New technologies such as microfluidic chips, advanced RFID tags and edible markers can detect contamination, help trace it back to its source and speed recalls.
- Government regulation of food production must be streamlined, but stiffer requirements by brand-name sellers on their suppliers will go further to ensure safer fare in the long run.

—The Editors

By Mark Fischetti

Given the billions of food items that are packaged, purchased and consumed every day in the U.S., let alone the world, it is remarkable how few of them are contaminated. Yet since the terrorist attacks of September 11, 2001, “food defense” experts have grown increasingly worried that extremists might try to poison the food supply, either to kill people or to cripple the economy by undermining public confidence. At the same time, production of edible products is becoming ever more centralized, speeding the spread of natural contaminants, or those introduced purposely, from farms or processing plants to dinner tables everywhere. Mounting imports pose yet another rising risk, as recent restrictions on Chinese seafood containing drugs and pesticides attest.

Can the tainting of what we eat be prevented? And if toxins or pathogens do slip into the supply chain, can they be quickly detected to limit their harm to consumers? Tighter production procedures can go a long way toward protecting the public, and if they fail, smarter monitoring technologies can at least limit injury.

Tighten Security

Preventing a terrorist or a disgruntled employee from contaminating milk, juice, produce, meat or any type of comestible is a daunting problem. The food supply chain comprises a maze of steps, and virtually every one of them presents an opportunity for tampering. Blanket solutions are unlikely because “the chain differs from commodity



to commodity,” says David Hennessy, an economics professor at Iowa State University’s Center for Agricultural and Rural Development. “Protecting dairy products is different from protecting apple juice, which is different from protecting beef.”

Even within a given supply chain there are few technology-based quick fixes. Preventing contamination largely comes down to tightening physical plant security and processing procedures at every turn. Each farmer, rancher, processor, packager, shipper, wholesaler and retailer “has to identify every possible vulnerability in the facility and in their procedures and close up every hole,” says Frank Busta, director of the National Center for Food Protection and Defense at the University of Minnesota. The effort begins with standard facility access controls,

which Busta often refers to as “gates, guns and guards,” but extends to thoroughly screening employees and carefully sampling products at all junctures across the facility at all times.

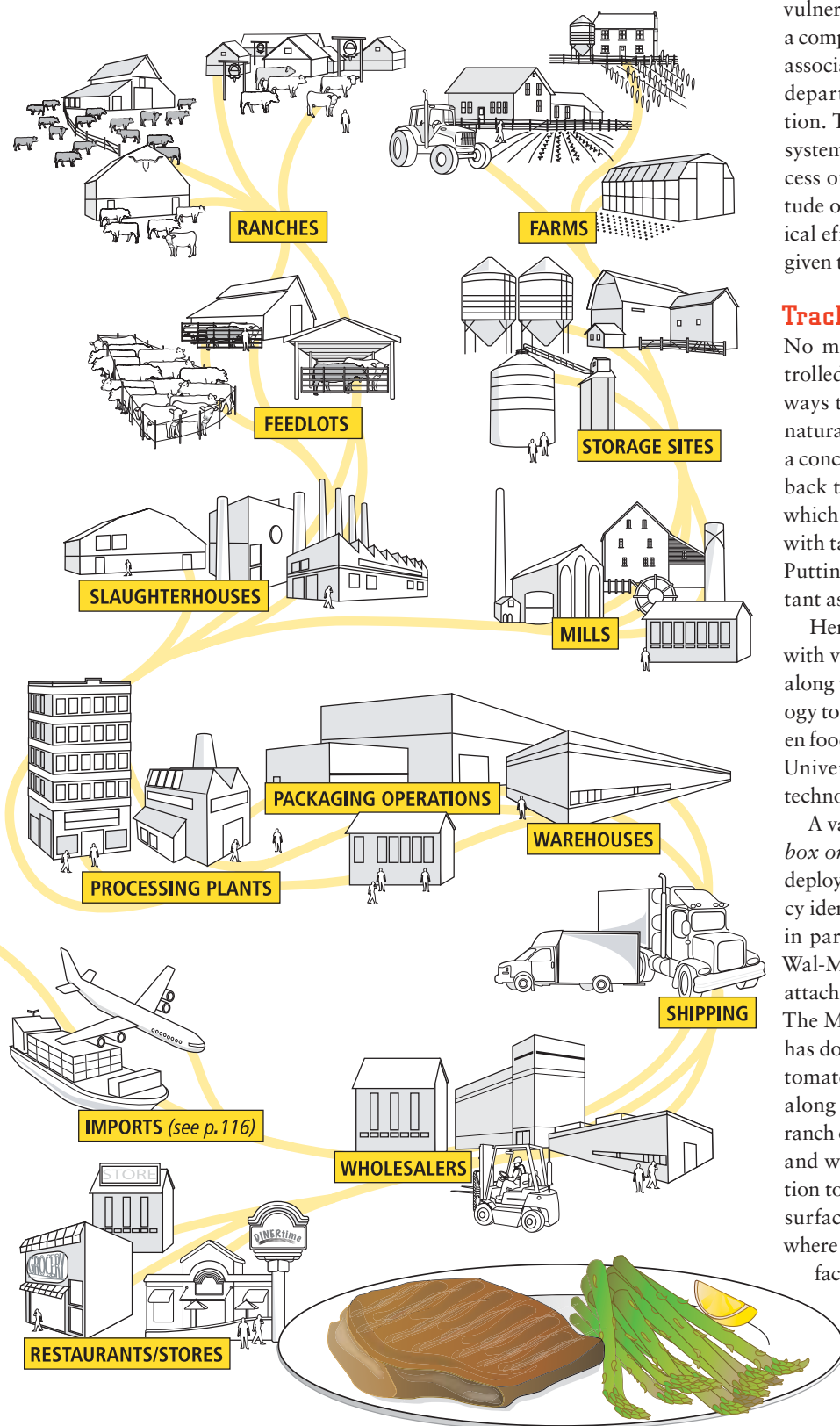
That advice seems sound, of course, but the challenge for operators is how best to button down procedures. Several systems for safeguarding food production have been rolled out in recent years. Though these are not required by any regulatory agency, Busta strongly recommends that producers implement them. In the U.S., that impetus has been made stronger by legislation such as the 2002 Bioterrorism Act and a 2004 presidential directive, both of which require closer scrutiny of ingredient suppliers and tighter control of manufacturing procedures.

The primary safeguard systems Busta recommends borrow from military practices. The

[THE PROBLEM]

Vulnerabilities Everywhere

The food supply chain includes numerous steps where natural pathogens can multiply or where terrorists or disgruntled employees could introduce toxins. Tight security and production procedures at myriad facilities are the primary countermeasures.



newest tool, which the FDA and the U.S. Department of Agriculture are now promoting, carries the awkward name of CARVER+Shock. It is being adapted from Defense Department procedures for identifying a military service's greatest vulnerabilities. "CARVER+Shock is essentially a complete security audit," says Keith Schneider, associate professor at the University of Florida's department of food science and human nutrition. The approach analyzes every node in the system for factors that range from the likely success of different kinds of attacks to the magnitude of public health, economic and psychological effects (together, the "shock" value) that a given type of infiltration could cause.

Track Contaminants

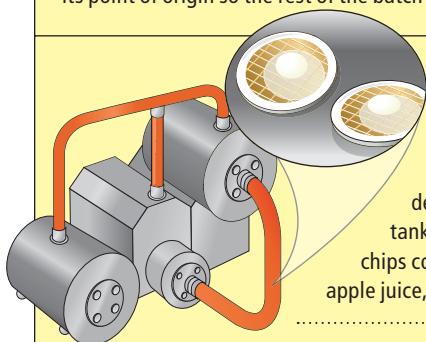
No matter how tightly procedures are controlled, determined perpetrators could still find ways to introduce pathogens or poisons. And natural pathogens such as salmonella are always a concern. Detecting these agents, tracing them back to the spot of introduction, and tracking which grocery stores and restaurants ended up with tainted products are therefore paramount. Putting such systems in place "is just as important as prevention," Schneider says.

Here new technology does play a major role, with various sensors applied at different points along the chain. "You can't expect one technology to counter all the possible taintings for a given food," notes Ken Lee, chairman of Ohio State University's department of food science and technology.

A variety of hardware is being developed [see box on opposite page], although little has been deployed commercially thus far. Radio-frequency identification (RFID) tags are furthest along, in part because the Defense Department and Wal-Mart have required their main suppliers to attach the tokens to pallets or cases of foodstuffs. The Metro AG supermarket chain in Germany has done the same. The ultimate intent is for automated readers to scan the tags at each step along the supply chain—from farm, orchard, ranch or processor, through packaging, shipping and wholesale—and to report each item's location to a central registry. That way if a problem surfaces, investigators can quickly determine where the batch originated and which stores or facilities might have received goods from that batch and when. Retailers can also read the tags on their items to see if they have received a product later identified as suspicious.

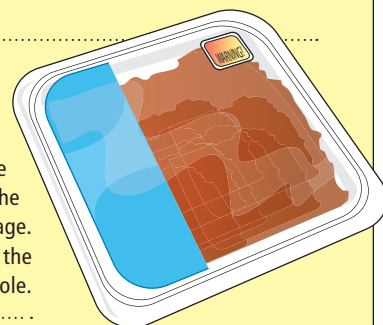
DETECT, TRACK AND TRACE

If a natural pathogen, or a perpetrator, contaminates food, lives will be saved if the tainted product can be quickly detected, then traced back to its point of origin so the rest of the batch can be tracked down or recalled. The following technologies, in development, could help:



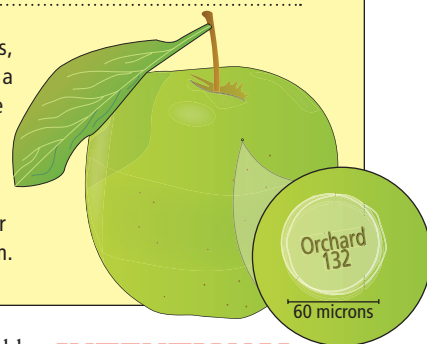
◀ **MICROFLUIDIC DETECTORS**—Botulinum bacteria produce the most poisonous toxin known. They and similar agents, such as tetanus, could be detected during food processing by microfluidic chips—self-contained diagnostic labs the size of a finger. The University of Wisconsin—Madison is crafting such a chip, lined with antibodies held in place by magnetic beads, that could detect botulism during milk production. The chip could sample milk before or after it was piped into tanker trucks that leave the dairy and before or after it was pasteurized at a production plant. Other chips could detect other toxins at various fluid-processing plants, such as those that produce apple juice, soup or baby formula.

▶ **ACTIVE PACKAGING**—*E. coli*, salmonella and other pathogens could be detected by small windows in packaging, such as the cellophane around meat or the plastic jar around peanut butter. The “intelligent” window would contain antibodies that bind to enzymes or metabolites produced by the microorganism, and if that occurred the patch would turn color. The challenge is to craft the windows from materials and reactants that can safely contact food. Similar biosensors could react if the contents reached a certain pH level or were exposed to high temperature, indicating spoilage. And they could sense if packaging was tampered with, for example, by reacting to the pressure imposed by a syringe or to oxygen seeping in through a puncture hole.



◀ **RFID TAGS**—Pallets or cases of a few select foods now sport radio-frequency identification (RFID) tags that, when read by a scanner, indicate which farm or processing plant the batch came from. Future tokens that are smaller, smarter and cheaper could adorn individual packages and log every facility they had passed through and when. The University of Florida is devising tags that could be read through fluid (traditional designs cannot) and thus could be embedded inside the wall of sour cream or yogurt containers. The university is also developing active tags that could record the temperatures a package had been exposed to.

▶ **EDIBLE TAGS**—Manufacturers often combine crops from many growers, such as spinach leaves, into a retail package, so tags affixed to bags might not help investigators track contamination back to a specific source. ARmark Authentication Technologies can print microscopic markers that indicate site of origin directly onto a spinach leaf, apple or pellet of dog food using a spray made from edible materials such as cellulose, vegetable oil or proteins. Also, the tiny size would be hard for terrorists to fake, making it harder for them to sneak toxin-laced counterfeit foods past inspectors and into the supply. As an alternative, DataLase can spray citrus fruits or meats with an edible film in a half-inch-diameter patch that is then exposed to a laser beam that writes identification codes within the film.



As RFID tags get smaller and cheaper, they will be placed directly on individual items—on every bag of spinach, jar of peanut butter, container of shrimp and sack of dog food. “That way if a recall is issued, the items can be found as they run past a scanner at the checkout counter,” says Jean-Pierre Émond, professor of agricultural and biological engineering at the University of Florida.

Universities and companies are developing all kinds of other tags, some that are very inexpensive and others that cost more but supply extensive information. Some tokens, for example, can sense if food has been exposed to warm temperatures and thus might be more likely to harbor

Escherichia coli or salmonella. Other tags could track how long items spent in transit from node to node in the supply chain, which could indicate unusually long delays that might raise suspicion about tampering. So-called active packaging could detect contamination directly and warn consumers not to eat the product they are holding.

The big impediment for any marker, of course, is the price. “Right now it costs 25 cents to put an RFID tag on a case of lettuce,” Emond notes. “But for some growers, that equals the profit they’re going to make on that case.”

To be embraced widely, therefore, he says tags will have to provide additional value to suppli-

INTENTIONAL POISONINGS

U.S., 1984,
salmonella in salad bars,
by Rajneeshees cult,
751 sickened

CHINA, 2002,
rat poison in breakfast foods,
by competitor to the vendor,
400 sickened, over 40 killed

U.S., 2002,
nicotine sulfate in ground beef,
by disgruntled worker,
111 sickened

The U.S. imports 50 percent more food than it did just five years ago.

ers or buyers. His university has been conducting an ongoing project with Publix Super Markets and produce suppliers in Florida and California to assess the possibilities. In initial trials, tags tracked crates and pallets that were shipped from the growers to several of Publix's distribution centers. Information gleaned from scanning tags at various points was available to all the companies via a secure Internet site hosted by VeriSign, the data security firm. The compilation allowed the participants to more quickly re-

solve order discrepancies, to log how long food sat idle, and to reveal ways to raise shipping efficiency. The group plans to extend the test to retail stores.

Control Suppliers

Costs will not drop until new technologies are widely deployed, but food defense analysts say adoption is unlikely to occur until clear, streamlined regulations are enacted. That prospect, in turn, will remain remote until the highest levels

[POLICY SOLUTIONS]

MAKING IMPORTS SAFER

Alarming warnings about Chinese products in recent months have shown how dangerous imported edibles can be. In March some 100 brands of pet food were recalled after they were found to contain melamine, a toxic chemical used as a cheap replacement for wheat gluten. Then in June the U.S. Food and Drug Administration issued alerts about five types of seafood that contained antibiotic residues, pesticides and salmonella.

After the seafood scare, Senator Charles Schumer of New York declared that the federal government should establish an import czar. He blamed poor control of imports on a lack of inspection and poor regulation, telling the *Washington Post* that "neither the Chinese or American government is doing their job."

Regardless of how safe domestic production is, "imports are our Achilles' heel," says Ken Lee, chairman of Ohio State University's department of food science and technology. "There is no global food regulator. If the Chinese want to put an adulterant into food, they can do it until they get caught. I'll wager it will happen again, because it's driven by the profit motive."

Realistically, no technology can ensure that imports are safe. The food in every shipping container entering a U.S. port or border crossing could be pulled and irradiated, and some comestibles such as spices are already processed this way. But industry says the step would add

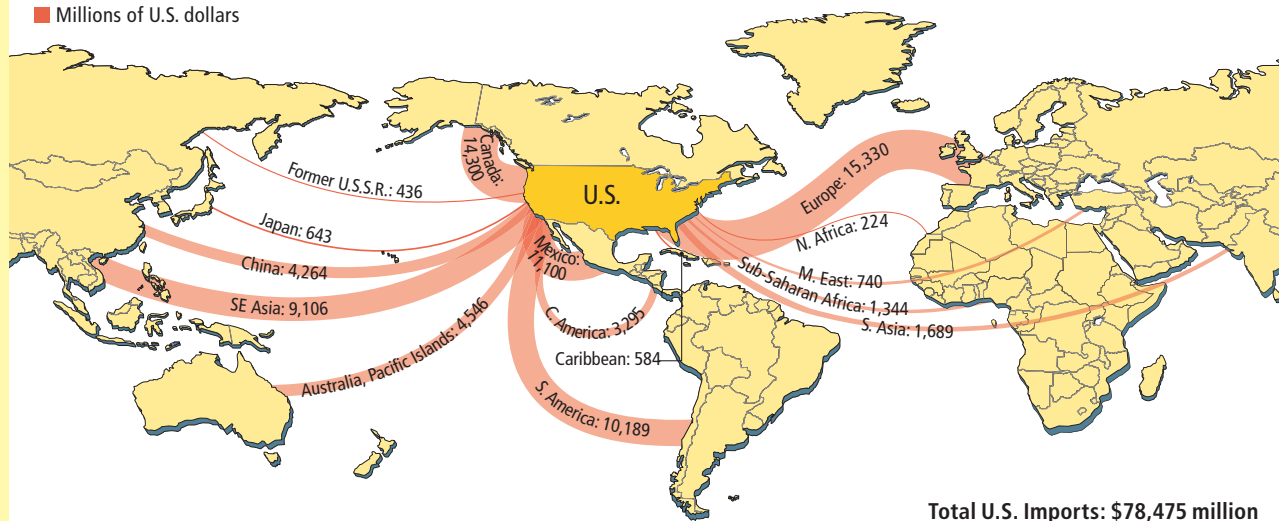
significant cost for producers and shipping delays for middlemen. And the public continues to be wary of the technology. Furthermore, although irradiation would kill pathogens, it would have no effect on poisons or adulterants.

Inspecting all incoming food would also require vast increases in FDA and U.S. Department of Agriculture budgets; the agencies currently inspect a meager 1 percent of imports. As a partial alternative, in June the FDA said it intended to conduct more inspections of products from countries it deems to have poorer food-safety controls, such as China, offset by fewer inspections of products from countries with stronger standards, such as Britain and Canada. The agency also said it might require importers and U.S. manufacturers that use imported ingredients to provide more detailed information about production processes at foreign suppliers.

The best recourse, Lee says, is for companies to insist that suppliers impose strict standards and that the companies send inspectors overseas to verify compliance. Other experts agree, adding that government edicts are not as effective. "Too often import requirements are used as trade barriers, and they just escalate," says David Hennessy, an economics professor at Iowa State University. "The food companies themselves have a lot to lose, however. When they source a product in a country, they ought to impose tough procedures there." —M.F.

U.S. AGRICULTURAL AND SEAFOOD IMPORTS, 2006

■ Millions of U.S. dollars

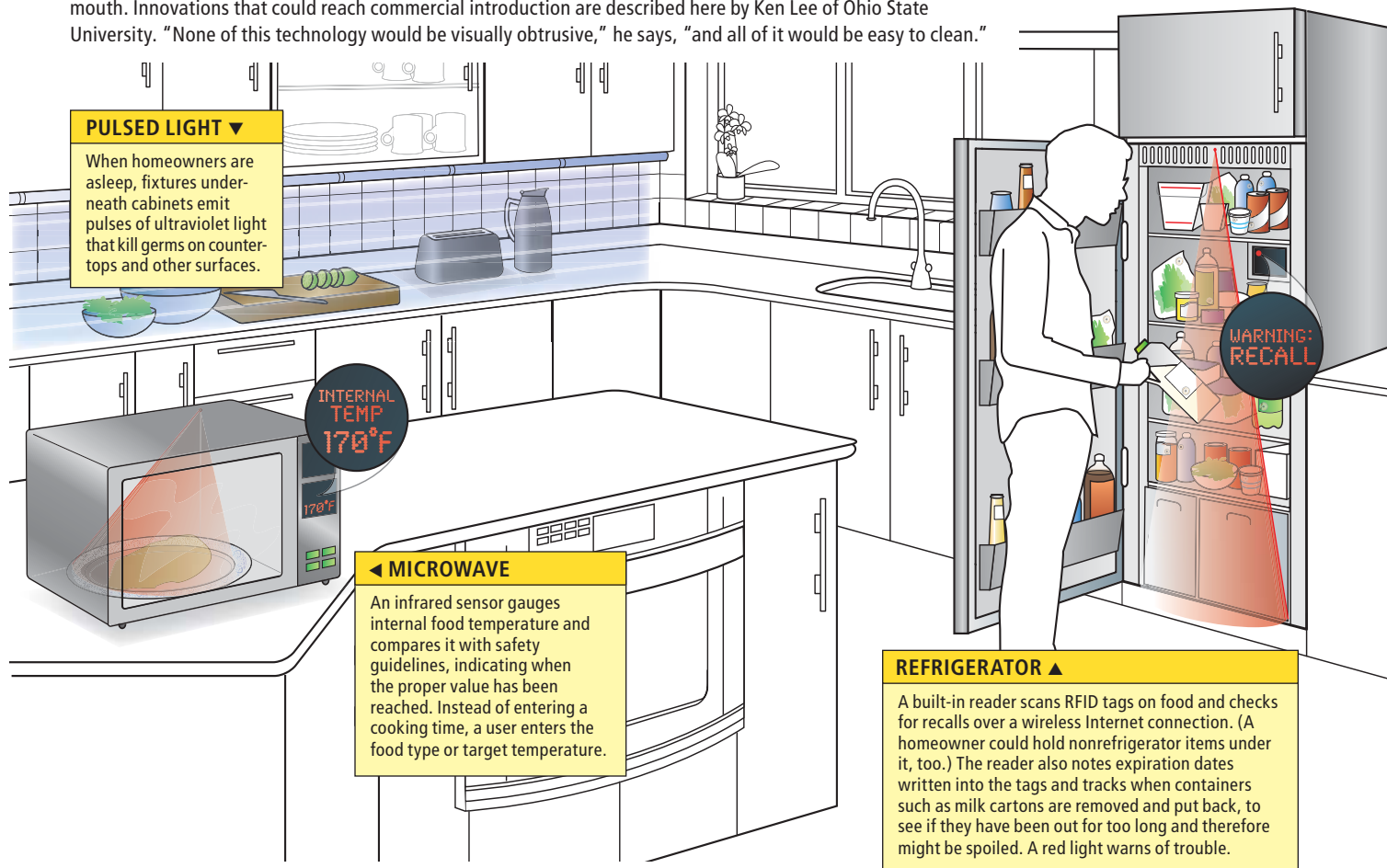


GEORGE RETSECK AND LUCY READING-IKKANDA; SOURCE: U.S. DEPARTMENT OF AGRICULTURE

[SAFETY AT HOME]

The Vigilant Kitchen

If contaminated food does make it into your grocery bag, smart appliances could still prevent it from reaching your mouth. Innovations that could reach commercial introduction are described here by Ken Lee of Ohio State University. "None of this technology would be visually obtrusive," he says, "and all of it would be easy to clean."



of government are reformed. "There are more than a dozen different federal agencies that oversee some aspect of food safety," Lee points out, noting that simple coordination among them is difficult enough, and efficient approval of sensible requirements is even harder to come by. The FDA regulates pizza with cheese on it, but the USDA regulates pizza if it has meat on it, quips Jacqueline Fletcher, professor of entomology and plant pathology at Oklahoma State University. "The requirements for organic farmers are different from those for nonorganic farmers."

Spurred by recent recalls, members of Congress have called for streamlining the regulation system. Illinois Senator Richard Durbin and Connecticut Representative Rosa DeLauro are advocating a single food-safety agency, but turf wars have hampered any progress toward that goal.

Concerned that more effective government is a long shot, experts say the responsibility for

improved vigilance falls largely on food suppliers. "The strongest tool for stopping intentional contamination is supply-chain verification," says Shaun Kennedy, deputy director of the National Center for Food Protection and Defense. That means a brand-name provider such as Dole or a grocery store conglomerate such as Safeway must insist that every company involved in its supply chain implement the latest security procedures and detection, track and trace technologies or be dropped if it does not. The brand company should also validate compliance through inspections and other measures. The impetus falls on the brand-name provider because it has the most to lose. If a natural or man-made toxin is found in, say, a bag of Dole spinach or a container of Safeway milk, consumers will shun that particular label. "If a brand-name company wants to protect its products," Kennedy says, "it should validate every participant in the chain, all the way back to the farm." ■

➔ MORE TO EXPLORE

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Analyzing a Bioterror Attack on the Food Supply: The Case of Botulinum Toxin in Milk. Lawrence M. Wein and Yifan Liu in *Proceedings of the National Academy of Sciences USA*, Vol. 102, No. 28, pages 9984–9989, July 12, 2005.

Biosecurity: Food Protection and Defense. Shaun P. Kennedy and Frank F. Busta in *Food Microbiology: Fundamentals and Frontiers*, third edition. Edited by Michael P. Doyle and Larry R. Beuchat. American Society for Microbiology Press, 2007.

National Center for Food Protection and Defense: www.ncfpd.umn.edu/

Fresh from the Sea

By Mark Fischetti

Seawater has been converted into drinkable freshwater for decades in the Middle East and in the Caribbean. Only a few major seawater desalination plants exist in the U.S.; the largest operates in Tampa, Fla., and a project twice the size is being developed in Carlsbad, Calif. But that number could grow quickly as millions of people move to coastal communities, which often have insufficient groundwater. “Almost 20 desalination plants are proposed for California alone,” says Tom Pankratz, a desalination consultant in Houston. Installations are being considered in Texas and Georgia, as are more in Florida.

On average, seawater contains about 35,100 milligrams per liter of dissolved solids, 99 percent of which are salts. The World Health Organization considers water potable when that level drops below 500 mg/L. Various processes can achieve the conversion, but today two contenders

together account for about 88 percent of worldwide capacity: multistage flash distillation and reverse osmosis.

Multistage flash distillation requires high-temperature steam, which is a plentiful by-product at fossil-fuel power plants. As a result, “almost every power plant in the Middle East has a multistage flash plant beside it,” Pankratz notes. Reverse osmosis installations, which are generally cheaper to construct but run on electricity instead, were not cost-competitive until the 1990s, when the membranes that extract the salt became more efficient and durable. Better filters for prescreening suspended particulates in seawater also extended membrane life.

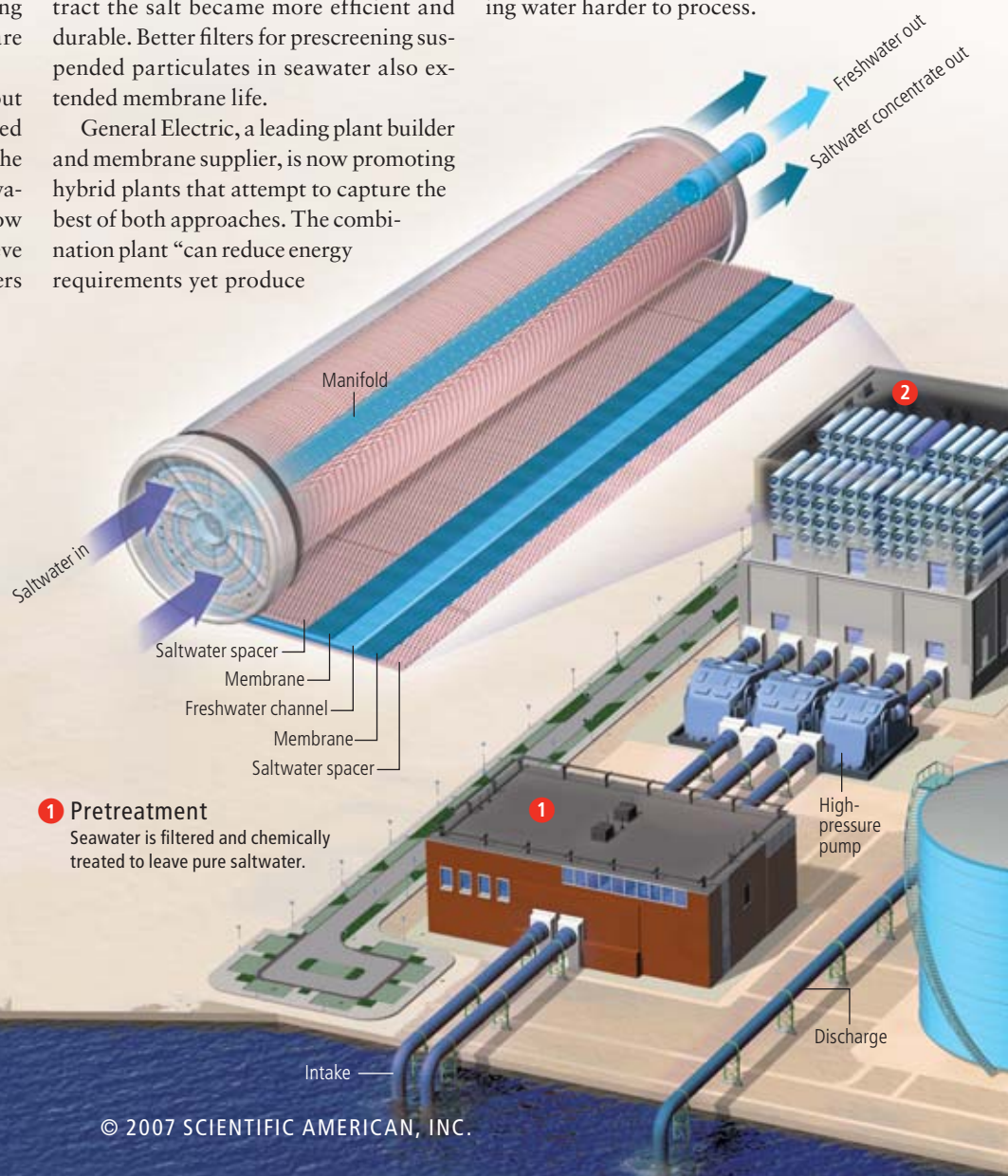
General Electric, a leading plant builder and membrane supplier, is now promoting hybrid plants that attempt to capture the best of both approaches. The combination plant “can reduce energy requirements yet produce

high-quality freshwater,” says Ralph Exton of GE in Trevose, Pa., who heads the company’s desalination projects in the Americas.

Some environmentalists have objected to desalination plants, claiming that the water intakes kill marine life and that the concentrated salt discharge alters the nearby seawater. But Pankratz says plant designers guard against both effects because they do not want fish clogging their systems and want to avoid raising local salinity because that would make incoming water harder to process.

→ REVERSE OSMOSIS

Pumps force saltwater against a semipermeable membrane. Freshwater passes through the membrane, but the dissolved salts do not. The freshwater is wicked into a central manifold and flows out; the remaining concentrated saltwater exits the system.

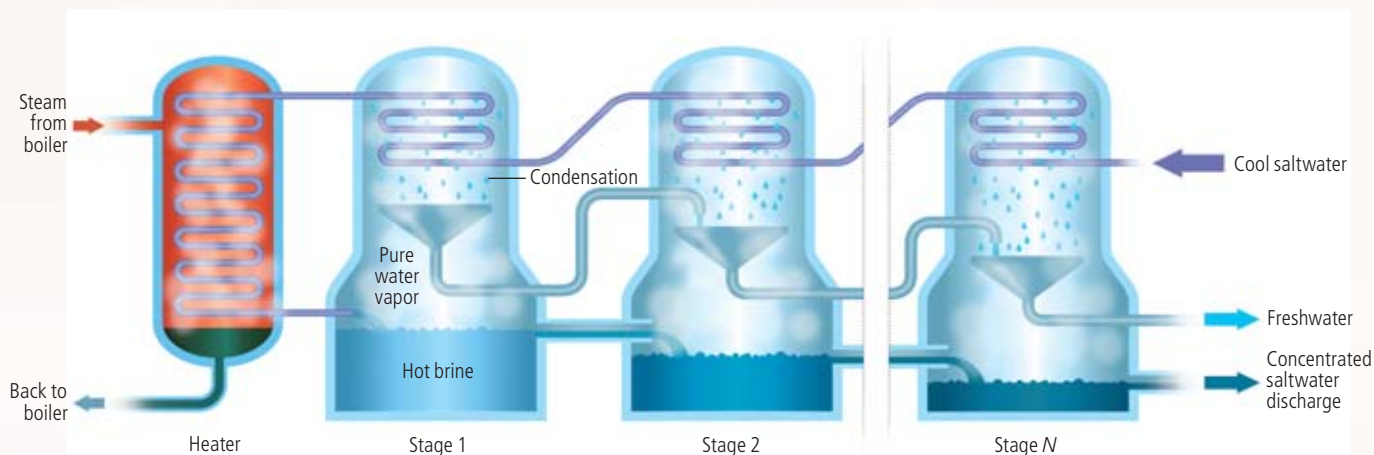


1 Pretreatment

Seawater is filtered and chemically treated to leave pure saltwater.

→ MULTISTAGE FLASH DISTILLATION

Cool saltwater warms as it passes through a series of distillation stages. A heater superheats it under pressure. When the liquid pours out into an open column that is at slightly lower pressure (stage 1), it flash-boils, sending pure water vapor upward, where it condenses into collectors. The adjacent column (stage 2) is kept at a lower pressure still, so the remaining saltwater flash-boils again, and so on (stage N) through many stages.

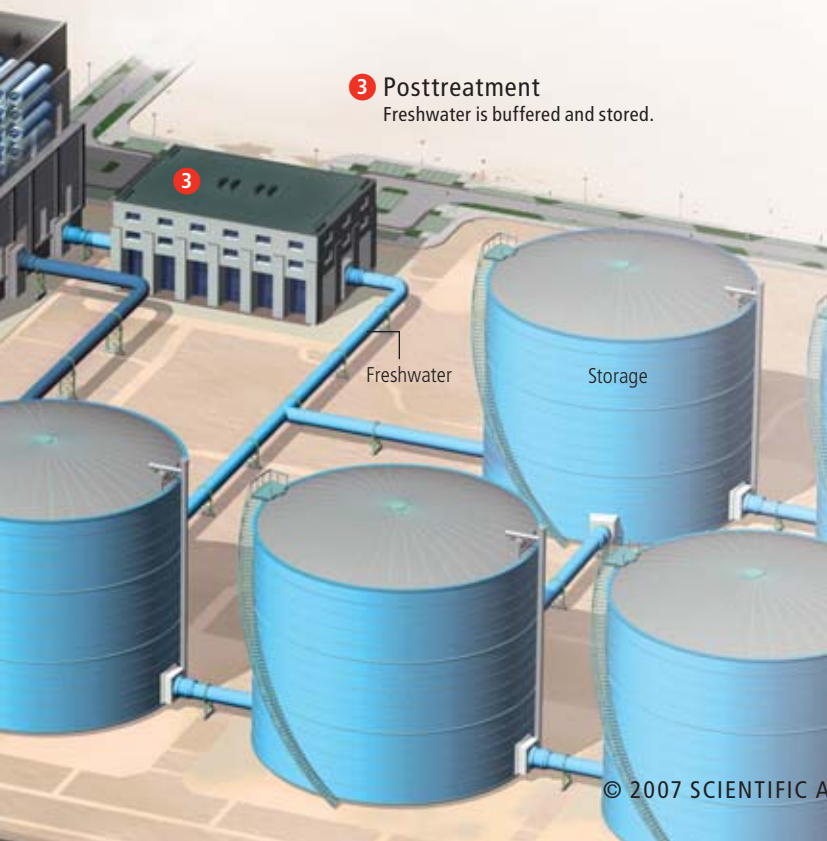


2 Desalination

Salt is removed via reverse osmosis (*detail at left*) or other processes such as flash distillation (*diagram above*). Concentrated saltwater discharge flows back to the ocean.

3 Posttreatment

Freshwater is buffered and stored.



DID YOU KNOW ...

SALTS IN WATER: Sodium chloride constitutes about 86 percent of the dissolved solids in seawater, magnesium sulfate accounts for 11 percent, and calcium bicarbonate and potassium bromide, about 1 percent each.

OCEANS APART: The average concentration of "total dissolved salts" in seawater ranges significantly, according to consultant Tom Pankratz: 33,300 milligrams per liter in the Pacific Ocean; 40,600 mg/L in the Mediterranean Sea; 48,000 mg/L in the Persian Gulf.

TASTE: Dissolved salts must be below 500 mg/L for water to qualify as potable. Pankratz says most people notice a disagreeable taste for concentrations nearing 1,000 mg/L or more. Yet if salts drop too low, people often say the water tastes flat or insipid.

GALLONS: Some 1,700 desalination plants in the Middle East convert 5.5 billion gallons of seawater a day, according to Global Water Intelligence. Capacity worldwide is 7.6 billion gallons daily.

IRAQ: The U.S. Army owns several thousand small trailers that can each produce up to 3,000 gallons a day of freshwater from saltwater, via reverse osmosis. Some are designed to be dropped by parachute and the army has done so routinely in Iraq.

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Cyclic Universe ■ World of Words ■ Nuclear Terror

BY MICHELLE PRESS

➔ **ENDLESS UNIVERSE: BEYOND THE BIG BANG**by Paul J. Steinhardt and Neil Turok.
Doubleday, 2007 (\$24.95)

The big bang theory holds that space and time sprang into existence 14 billion years ago from a hot, dense fireball. Paul J. Steinhardt and Neil Turok (well-known physicists at Princeton University and the University of

Cambridge, respectively) contend that the evolution of the universe is cyclic; big bangs occur once every trillion or so years, producing new galaxies, stars, planets and, presumably, life. They say they were motivated to form a new theory as the big bang came to require

more and more exotic elements—inflation, dark matter, dark energy—to make it fit observations. Their concept is still in its infancy, but, they say, writing an account now makes it possible to capture science as it is happening, through the eyes of scientists directly involved.

➔ **THE STUFF OF THOUGHT: LANGUAGE AS A WINDOW INTO HUMAN NATURE**

by Steven Pinker. Viking, 2007 (\$29.95)

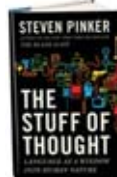
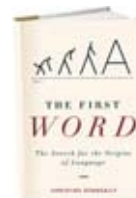
➔ **THE FIRST WORD: THE SEARCH FOR THE ORIGINS OF LANGUAGE**

by Christine Kenneally. Viking, 2007 (\$26.95)

Steven Pinker, who is a professor of psychology at Harvard University, probes the mystery

of human nature by examining how we use words, from the expected, such as swearing and innuendo, to the surprising. Prepositions and tenses, he says, for example, tap into our concepts of space and time. Pinker's own use of language continues to gather praise (he has twice been nominated for a Pulitzer Prize). His reputation was cinched when Stephen Colbert, on Comedy Central's *Colbert Report*, asked Pinker to explain how the brain works in

exactly five words, and he replied, "Brain cells fire in patterns." This book delivers his customary mix of interesting ideas and good writing, though not quite so succinctly.



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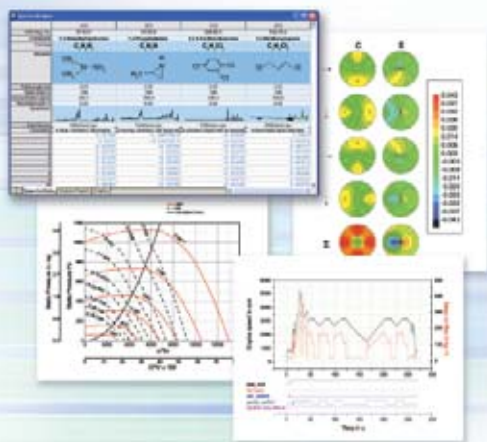
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Christine Kenneally, a linguist who writes about language, science and culture for the general public, sets into a much broader context the work of Pinker—with his collaborator, Paul Bloom—and that of three other leading language researchers (Noam Chomsky, Sue

Savage-Rumbaugh and Philip Lieberman). Her broader palette is the evolution of language. Is language a uniquely human phenomenon, she asks, or is it the product of a genetic framework, some of which we share with other communicating creatures such as apes and

the African grey parrot? In an elegant exposition, Kenneally takes us through the work of these experts and toward an answer.

EXCERPT

➔ THE ATOMIC BAZAAR: THE RISE OF THE NUCLEAR POOR

by William Langewiesche. Farrar, Straus and Giroux, 2007 (\$22)

Investigative journalist William Langewiesche tracks the proliferation of nuclear weapons, focusing his story on Pakistani scientist A. Q. Khan, who stole plans and equipment from the West and peddled the technology to countries hostile to Western interests:

"That same afternoon a small group of Pakistanis associated with the weapons program, including, of course, A. Q. Khan, gathered in a concrete bunker in Chagai, facing the chosen mountain seven miles away. Pakistan later reported that five nuclear bombs had been placed inside the test tunnel where it hooked sharply, eight hundred feet beneath the mountain's peak. The bombs were fission devices ... containing highly enriched uranium ... The tunnel was sealed with heavy concrete plugs. At 3:15 P.M. a PAEC technician ... pushed the button, saying, 'Allah-o-Akbar'—God is great. After a delay of thirty-five seconds (during which, it is said, some observers prayed) the mountain heaved, shrouding itself in dust. The command post rocked. When the dust settled, the mountain's color had turned to white. In announcing the news Pakistan claimed a total yield that roughly equaled India's, of course. Independent analysts downgraded the actual yield by a factor of three—but so what? As far away as Cairo, Muslims danced in the streets."

NEW AND NOTABLE BOOKS ON CLIMATE CHANGE

- 1 **Storm World: Hurricanes, Politics, and the Battle over Global Warming** by Chris Mooney. Harcourt, 2007 (\$26)
- 2 **Feeding the Fire: The Lost History and Uncertain Future of Mankind's Energy Addiction** by Mark E. Eberhart. Harmony Books, 2007 (\$24)
- 3 **The Winds of Change: Climate, Weather, and the Destruction of Civilizations** by Eugene Linden. Just out in paperback, with a new afterword that describes the accelerating crisis. Simon & Schuster, 2007 (paperback, \$15)
- 4 **Earth under Fire: How Global Warming Is Changing the World** by Gary Braasch. University of California Press, 2007 (\$34.95)



HIGH TIDE in Tuvalu, 2005

What is the *latest theory* of why humans lost their *body hair*?

—J. Yablon, Adelaide, Australia

Mark Pagel, head of the evolutionary biology group at the University of Reading in England, replies:

Scientists have suggested three main explanations for why humans lack fur. All revolve around the idea that it may have been advantageous for our evolving lineage to become less and less hairy during the six million years since we diverged from the common ancestor we shared with our closest living relative, the chimpanzee.

The “aquatic ape” hypothesis suggests that six million to eight million years ago, our apelike ancestors had a semiaquatic lifestyle, foraging for food in shallow waters. Fur is not an effective insulator in water, and so the theory asserts that we evolved to replace it, as other aquatic mammals have, with relatively high levels of body fat. Imaginative as this explanation is—and helpful in excusing our girth—paleontological evidence for an aquatic phase of human existence has proved elusive.

A second theory is that a loss of fur allowed for better control of our body temperature when we adapted to life on the hot savanna. Our ape ancestors spent most of their time in cool forests, but a furry, upright hominid walking around in the sun would have overheated. This idea seems sensible, but even though hairlessness might have made it easier to stay cool during the day, our ancestors also would have lost heat at night when they needed to retain it.

Recently my colleague Walter Bodmer of the University of Oxford and I suggested that natural selection favored nakedness because it reduced the prevalence of external parasites.

A furry coat provides an attractive safe haven for ectoparasites such as ticks, lice and biting flies.

These creatures not only bring irritation and annoyance but also carry an assortment of diseases, some of which can be fatal. Humans, being capable of building fires, constructing shelters and producing clothes,

would have been able to lose their fur, and thereby most of their parasites, without suffering from the cold.

How can an *opera singer* be heard over the much *louder orchestra*?

—A. Dean, Elgin, Ill.

John R. Smith, a physicist at the University of New South Wales in Sydney, Australia, explains:

Opera singers are able to maximize their sound output in frequencies where the orchestra is less powerful and to which the ear is more sensitive.

In both speech and singing, we produce sustained vowel sounds by using vibrations of our vocal folds—small flaps of mucous membrane in our voice box—that periodically interrupt the airflow from the lungs. The folds vibrate at a fundamental frequency, which determines the pitch: typically between 100 to 220 hertz (Hz), or vibrations per second, for normal speech and 50 to 1,500 Hz for singing. Speech and singing also contain a series of harmonics, which are basically multiples of that frequency. Singers, especially sopranos, can learn to tune the resonances of their vocal tract to match the fundamental frequency, providing a dramatic increase in acoustic power.

An orchestra is typically loudest around 500 Hz, with the sound level dropping off quickly at higher frequencies; the ear is most sensitive around 3,000 to 4,000 Hz. Many opera singers learn to increase the power in the harmonics at frequencies above 2,000 Hz, which helps to distinguish their voices.

Finally, opera singers often use much more vibrato—a slow, cyclic variation, or “wobble,” in pitch—than orchestral musicians do. This effect aids the signal processing within our auditory system in distinguishing the voice of a singer as something quite different from the accompaniment of the orchestra. ■

HAVE A QUESTION?... Send it to experts@SciAm.com or go to www.SciAm.com/asktheexperts



Do Living People Outnumber the Dead?

BY CIARA CURTIN

The human population has swelled so much that people alive today outnumber all those who have ever lived, says a rumor that has circulated for years. The rumor is an embellishment of one started in the 1970s, which asserted that 75 percent of all people ever born were alive at that time. In 1995 demographer Carl Haub of the Population Reference Bureau, a nongovernmental organization in Washington, D.C., addressed the issue by calculating how many people had ever existed, a number he updated in 2002. To arrive at the 2002 figure, he considered when humans first arose and estimated population growth rates during different historical periods.

Counting Everyone

Based on an estimate made in the 1973 United Nations report *Determinants and Consequences of Population Trends*, Haub assumed that the first *Homo sapiens* appeared around 50,000 years ago and counted the population at that time as two—his Adam and Eve.

Little is known about life that long ago, but by examining data from the U.N. and elsewhere, Haub calculated that by 8000 B.C., the time of the Middle East's agricultural revolution, the earth held some five million people.

Between the rise of farming and the height of Roman rule, population growth was sluggish; at a rate of less than a tenth of a percent per year, humanity's number crawled to about 300 million by A.D. 1. That total then fell as plagues wiped out large swaths of people. (The Black Death in the 14th century wiped out at least 75 million.) As a result, by 1650 the world population had increased only to about 500 million. But by 1850 it doubled to more than one billion thanks to improved agriculture and sanitation. And by 2002 the planet's population had exploded, reaching 6.2 billion.

Together such figures revealed that slightly more than 106 billion people had ever been born. Of that number, those alive in 2002 constituted only about 6 percent. (See www.prb.org/

Articles/2002/HowManyPeopleHaveEverLivedonEarth.aspx for more details on Haub's math.) Today more than 6.5 billion people inhabit the planet, according to the U.N. "[It is] almost surely true people alive today are some small fraction of [all] people," says Joel E. Cohen, a professor of populations at the Rockefeller University and Columbia University. For the myth to be valid now, more than 100 billion would have to be alive.

Myth Today, Truth Tomorrow?

What about the future? Recently the population has been increasing by about 1.2 percent each year, down from the late 1960s peak of about 2 percent. Some industrial countries, such as Japan, have very low birth rates, and their populations are actually dwindling, Haub notes. In developing nations, populations continue to grow, although some countries, such as India, are experiencing a slowdown in their growth rates.

Cohen doubts that a doubling of today's population, to 13 billion, will ever occur, never mind its approaching anywhere near 100 billion. Not even the U.N.'s highest projection foresees that much growth, he says. For 2050, the world body's estimates range from 7.3 billion to 10.7 billion people. The median, and most likely, projection of 8.9 billion relies on a gradual slowing of the growth rate. And the U.N. has anticipated that the world population will stabilize at 10 billion inhabitants sometime after 2200. At this rate, the living will never outnumber the dead. ■

Ciara Curtin is a freelance science journalist based in New York City.

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